Hypertensive Disorders of Pregnancy

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Outline

- Definitions and Diagnosis
  - 2013 Hypertensive Task Force Recommendations
- Pathophysiology and manifestations
- Evaluation and Management
  - Initial evaluation
  - Expectant Management of “Mild” and “Severe” Disease
  - Outpatient versus inpatient management
  - Timing of delivery
- Prediction and Prevention

Executive Summary: Hypertension in Pregnancy

American College of Obstetricians and Gynecologists

Obstet Gynecol 2013;122:1122-31

ACOG Executive Summary on Hypertension In Pregnancy, Nov 2013

1. The term “mild” disease is no longer appropriate terminology. The recommended terminology is:
    a. “**preeclampsia without severe features**” (mild)
    b. “**preeclampsia with severe features**” (severe**)**

2. Proteinuria **is not** a requirement to diagnose preeclampsia with **new onset** hypertension.

3. The **total** amount of proteinuria has been eliminated from the diagnosis of severe preeclampsia (no association with maternal/fetal outcome).

ACOG Executive Summary on Hypertension In Pregnancy, Nov 2013

4. Early treatment of **severe** hypertension is mandatory at the threshold levels of **160 mm Hg** systolic or **110 mm Hg** diastolic.

5. Magnesium sulfate for seizure prophylaxis is **indicated** for **severe** preeclampsia and **could** be administered universally for preeclampsia without severe features (mild)*.

Criteria for Pre-eclampsia Diagnosis

- Systolic blood pressure of ≥140 mmHg or diastolic blood pressure ≥90 mmHg on two occasions at least 4 hrs apart after 20 weeks in a previously normotensive pt

AND

- Proteinuria ≥0.3 gms in 24 hrs or P/C ratio ≥0.3
- Dipstick +1 if quantitative is unavailable
  - false positive rate of 71%
  - +3 has 7% false positive rate
- If systolic blood pressure is ≥160 mmHg or diastolic is ≥110 mmHg, confirmation within minutes is sufficient and do not *need* proteinuria

Criteria for Diagnosis: Severe Disease

- **Symptoms of central nervous dysfunction**
  - New onset cerebral or visual disturbances such as
    - Photopsia, scotomata, cortical blindness, retinal spasms
    - Severe HA or HA that persists and progresses despite analgesia
    - Altered mental status
- **Hepatic Abnormalities**
  - Severe persistent RUQ or epigastric pain unresponsive to medication and not accounted for by an alternative diagnosis OR serum transaminases twice the upper limit of normal, or both
- **Severe Blood Pressure Elevations**
  - See previous slide
- **Thrombocytopenia**
  - < 100,000 plts/microliter
- **Renal abnormalities**
  - Serum Cr > 1.1 mg/dL or doubling from baseline
- **Pulmonary Edema**

Additional Definitions

- **Eclampsia** – development of grand mal seizures in the absence of other causes
  - MRI studies: permanent white matter loss in 25% of those affected
  - up to 38% do not have proteinuria or hypertension

- **HELLP** – **H**emolysis, **E**levated **L**iver enzymes, **L**ow **P**latelets
  - LDH > 600, AST/ALT twice normal, plts < 100K
  - Up to 15-20% are without hypertension or proteinuria
  - Main presenting symptoms: RUQ pain and generalized malaise (90%), nausea and vomiting 50%

- **Chronic hypertension** – the existence of elevated blood pressures (140 mmHg systolic and/or 90 mmHg diastolic) prior to pregnancy or prior to 20 weeks

- **Preeclampsia superimposed on chronic hypertension (SIPE)** – new-onset of either proteinuria or end-organ dysfunction after 20 weeks gestation in a previously hypertensive woman

- **Gestational hypertension** – Hypertension without proteinuria or without signs of end-organ dysfunction that develops after 20 weeks and resolves postpartum.

Differential Diagnosis

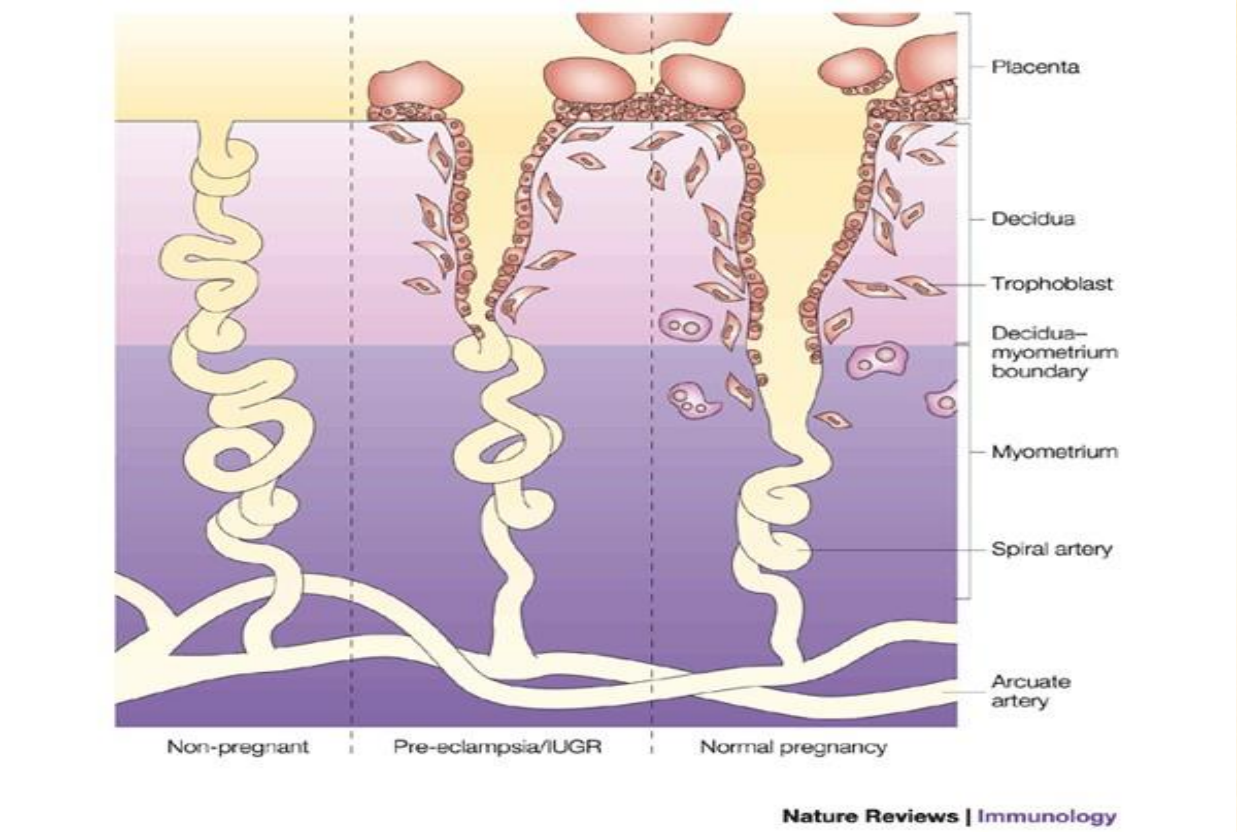
Frequency and severity of laboratory findings among imitators of preeclampsia-eclampsia

Laboratory findings	HELLP syndrome	AFLP	TTP	HUS	Exacerbation of SLE
Thrombocytopenia (less than 100,000/mm^3)	More than 20,000	More than 50,000	20,000 or less	More than 20,000	More than 20,000
Hemolysis (percent)	50-100	15-20	100	100	14-23 with APA
Anemia (percent)	Less than 50	Absent	100	100	14-23 with APA
DIC (percent)	Less than 20	50-100	Rare	Rare	Rare
Hypoglycemia (percent)	Absent	50-100	Absent	Absent	Absent
VW factor multimers (percent)	Absent	Absent	80-90	80	Less than 10
ADAMTS13 less than 5 percent (percent)	Absent	Absent	33-100	Rare	Rare
Impaired renal function (percent)	50	90-100	30	100	40-80
LDH (IU/L)	600 or more	Variable	More than 1000	More than 1000	With APA
Elevated ammonia (percent)	Rare	50	Absent	Absent	Absent
Elevated bilirubin (percent)	50-60	100	100	NA	Less than 10
Elevated transaminases (percent)	100	100	Usually mild*	Usually mild*	With APA

HELLP: hemolysis, elevated liver enzymes, low platelets; AFLP: acute fatty liver of pregnancy; TTP: thrombotic thrombocytopenic purpura; HUS: hemolytic uremic syndrome; SLE: systemic lupus erythematosus; APA: antiphospholipid antibodies with or without catastrophic antiphospholipid syndrome; DIC; disseminated intravascular coagulopathy; VW: von Willebrand; ADAMTS: von Willebrand factor-cleaving metalloprotease; LDH: lactic dehydrogenase; NR: values are not available.
* Levels less than 100 IU/L.

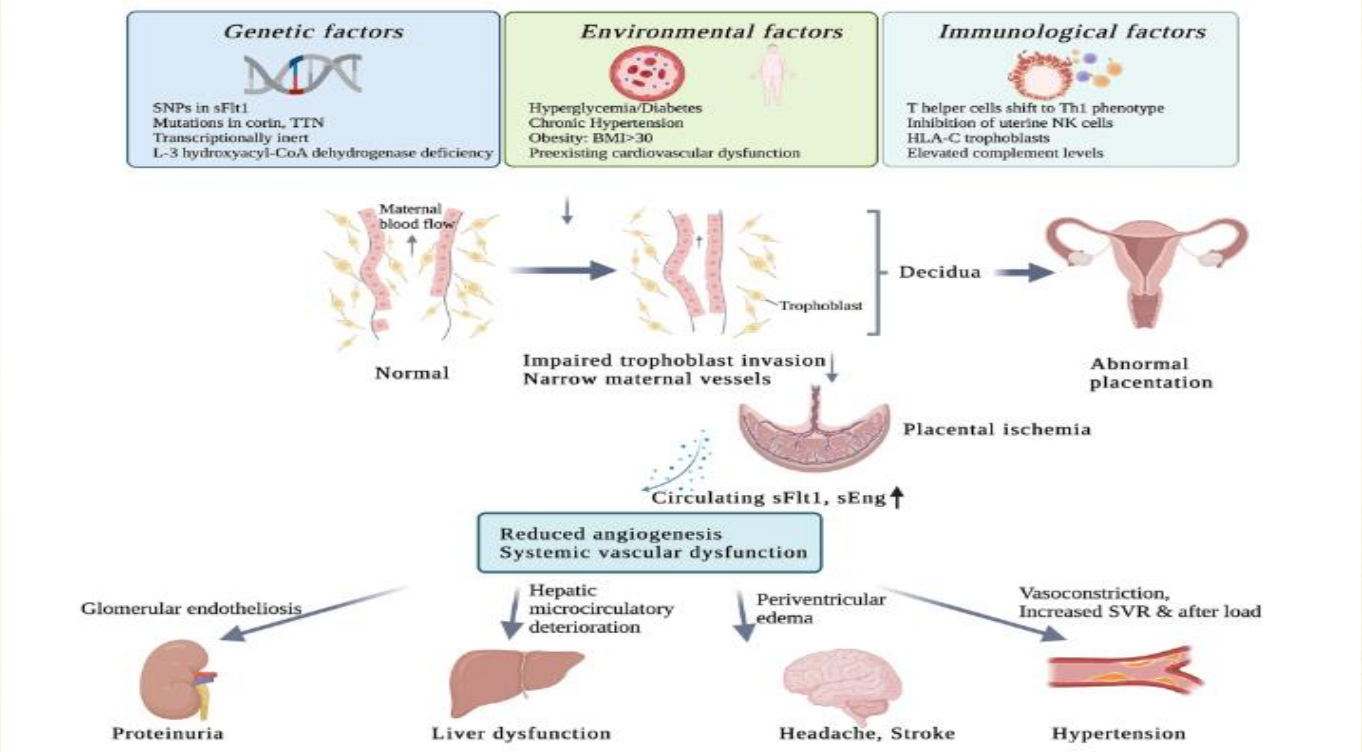
Pathophysiology

- Multi-system progressive disorder characterized by new-onset hypertension > 20 weeks in a previously normotensive woman
- Continues to be one of the leading causes of mortality in US
- Etiology is likely both maternal and fetal/placental



Pathophysiology

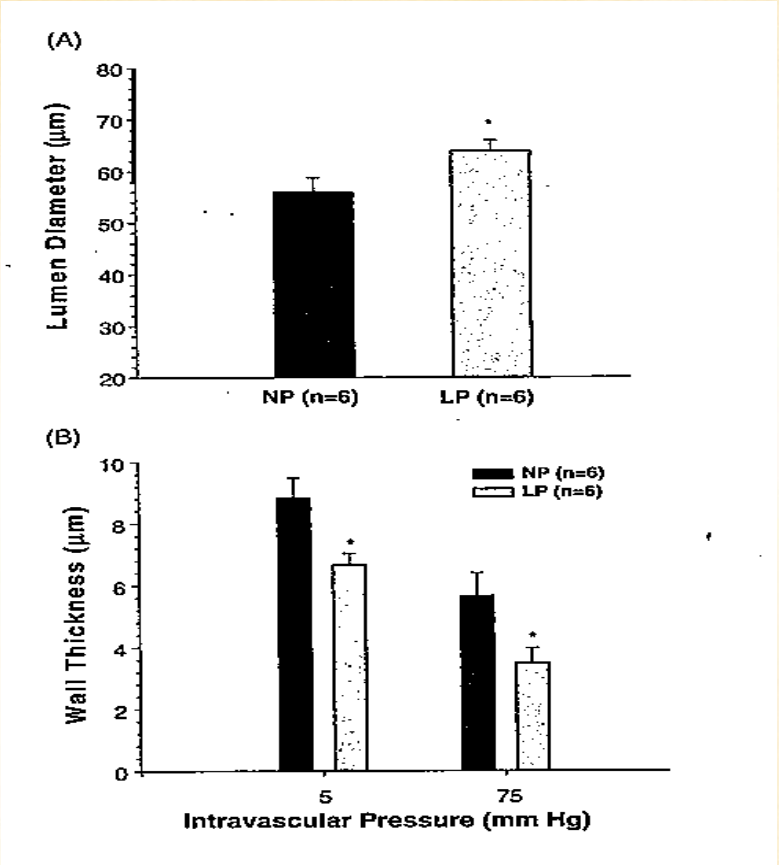
Abnormal trophoblast invasion (immunologic factors??)➔ small caliber, responsive spiral arteries ➔ placental hypoperfusion and hypoxia ➔ release of anti-angiogenic factors (sFlt-1)➔ alteration of systemic endothelial function ➔ HYPERTENSION

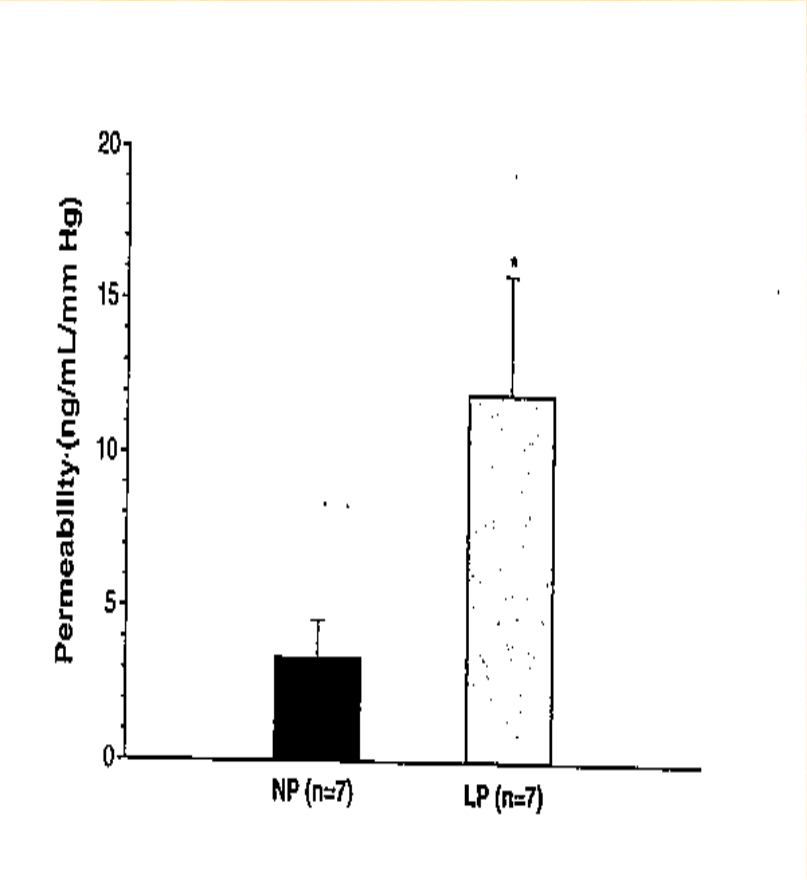


Pathophysiology by organ system

- **Cerebrovascular changes**
  - ***Visual changes*** are precipitated by retinal arterial spasms
    - Photopsia – flashing lights or sparks
    - Scotomata – dark spots in vision
    - Amaurosis fugax – blindness in one/both eyes (curtains coming down over eyes)
    - Retinal detachment
  - ***Headaches***
    - Increase in intracerebral pressure ➔ overcomes autoregulation ➔ areas of forced vasodilation and constriction ➔ increased hydrostatic pressure and vasogenic edema (PRES syndrome)
  - ***Eclampsia***
    - Excessive release of excitatory neurotransmitters (glutamate), massive depolarization and bursts of action potentials
    - 1 in 400 without severe disease
    - 1 in 50 with severe disease
  - ***Stroke***
    - Cerebral hemorrhage (either primary or a transformed ischemic area)
    - Preeclampsia-related strokes are responsible for 36% of all pregnancy-related strokes

Cerebral Vascular Changes





Cipolla MJ et al. Pregnancy decreases myogenic acitivity of brain parenchymal arterioles: Role of

Pathophysiology by organ system

- **Cardiovascular alterations**
  - Intense vasospasm (thromboxane A2, endothelins) → must be VERY careful with aggressive fluid correction
  - Increased afterload/systemic vascular resistance
    - Shift from normal pregnancy to a low output, high resistance state
      - Lower cardiac output (Visser et Wallenburg, 1991)
    - Lower heart rate
      - CO = SV x HR
- **Volume/hematologic alterations**
  - Pregnancy = increase in 50% of blood volume
    - Preeclampsia → endothelial damage → capillary leak
  - Low platelets
    - Microangiopathic endothelial injury → plt and fibrin thrombi → plt consumption
    - Immune component?
  - No effect on PT, PTT and fibrinogen
    - Periportal flow decreased → infarction → hemorrhage
      - Transient diabetes insipidus
  - Microangiopathic hemolysis
    - Peripheral smear → schistocytes

Pathophysiology by organ system

- **Renal alterations**
  - Renal vasoconstriction
  - Decreased GFR (30-40%) as compared to normotensive pregnant women
  - An increase in serum creatinine
  - Increased uric acid (both increased production and decreased excretion)
    - Predictive of adverse perinatal outcome, but not maternal outcomes (Livingston JR et al, J Obstet Gynecol Can 2014)
  - Renal histologic changes
    - “glomerular endotheliosis”

What about Fetal Effects?

- Chronic placental hypoperfusion
  - Changes in cord dopplers
  - Intrauterine growth restriction (25% in early onset disease)
  - Oligohydramnios

  **Note: these are no longer part of the criteria for severe disease*
- Indicated preterm birth
- Abruption (3% of those with severe disease)

Complications of preeclampsia

Outcome measure	Normal blood pressure, (percent)	Mild preeclampsia (percent)	Severe preeclampsia (percent)
Maternal			
Liver dysfunction	0.2	3.2	20.2
Kidney dysfunction	0.3	5.1	12.8
Placental abruption	0.7	0.5	3.7
Induced labor	12.1	41.5	58.7
Cesarean delivery	13.3	30.9	34.9
Delivery <34 weeks	3.2	1.9	18.5
Fetal or neonatal			
Growth restriction	4.2	10.2	18.5
Admission to NICU	12.9	27.3	42.6
Respiratory difficulty	3.8	3.2	15.7
Brain hemorrhage	0.2	0.5	0
Fetal death	0.9	0.5	0.9
Neonatal death	0.5	0.5	0.9

Adapted from data in Hauth, JC, Ewell, MG, Levine, RJ, et al. Obstet Gynecol 2000; 95:24.

Graphic 54736 Version 1.0

Risk Factors

- Nulliparity (NOT HELLP) – RR 2.9
- Previous pregnancy with PEC
  - 25-65% if severe, early onset
  - 5-7% without severe features
  - 1% if normotensive
- > 40 y/o or < 18 y/o
- Family history of PEC (RR 2.9)
- cHTN (RR 1.38-2.37)
- Preexisting medical condition (diabetes RR 3.56, renal disease)
- APLS
- Vascular disease

- Multifetal gestation (RR 2.9)
- High BMI (RR 2.47)
- Black Race
- Male partner whose mother or previous partner had PEC
- IUGR
- Woman herself was IUGR
- IURG, abruption or IUFD in previous pregnancy
- Partner related factors
- Hydatiform mole

Clinical Manifestations

- 90% of women present after 34 weeks (late-onset)
- 5% develop symptoms in the postpartum
- 2% develop eclampsia
  - 20-30% will seize without evidence of blood pressure elevations
- Degree of HTN, proteinuria and presence/absence of symptoms can be variable
  - Up to 25% will develop 1 or more severe symptoms and require delivery
- Atypical presentation
  - Twins or multiples
  - Presentation prior to 20 weeks

Initial Evaluation

- **<u>Thorough history and physical examination</u>**
  - *Fetal Evaluation*
    - NST (any elevations in BP should prompt putting fetus on monitor)
    - US for fetal position, AFI, dopplers and growth
  - *CV exam*
    - Hypertension??
      - Cycle blood pressure every 15-30 min depending on the initial evaluation
    - Chest pain can be a sign of cardiovascular ischemia in women with severe disease
    - Could be confused for “heart burn”
  - *Pulmonary exam* – pulse ox meter, signs of pulm edema?
    - Elevated pulmonary hydrostatic pressures with low oncotic pressures ➔ fluid into lungs
    - Can also be secondary to capillary leak, heart failure, fluid overload (if on IV hydration)

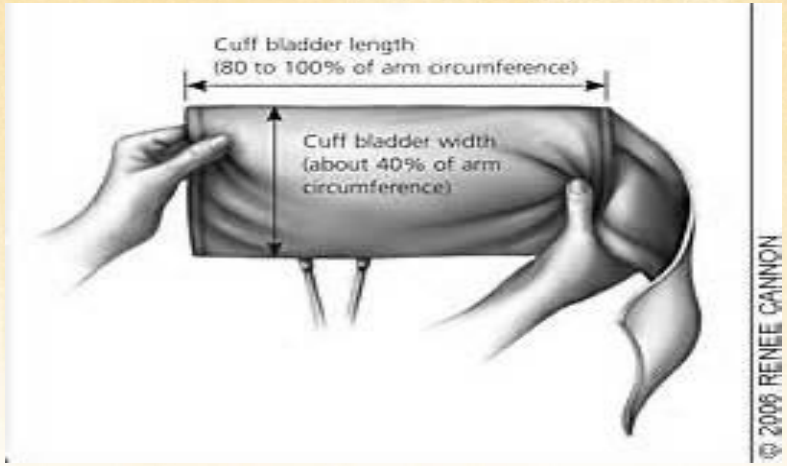
Initial Evaluation

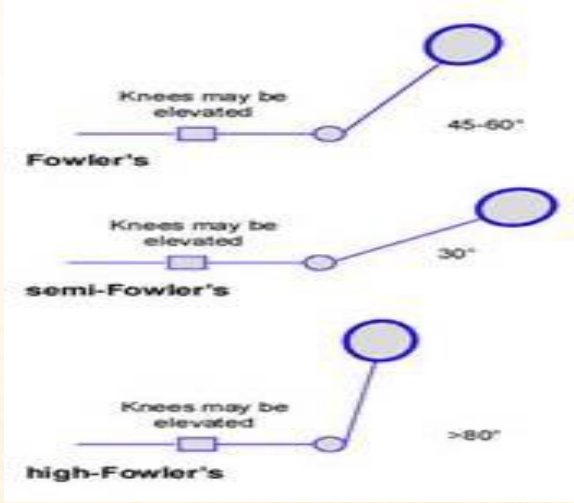
- **<u>Thorough history and physical examination</u>**
  - *Abdominal Exam* – palpate the liver, ask about pain
    - Epigastric pain not relieved with meds
  - *Neurologic Exam* – check reflexes and clonus
    - Headaches – how long? Location? Relief with analgesics?
    - Visual changes – blurry, cloudy, spots, or change in vision?
  - *HEENT* – facial swelling?
  - *Extremities* – Clonus? Reflexes
    - Edema – ask about recent rapid weight gain
      - Likely due to
        - Capillary leak
        - Endothelial damage
        - Low oncotic pressure

Proper Blood Pressure Evaluation

- Mercury sphygmomanometer is gold standard
  - Automated can underestimate by as much as 10 mmHg (Natarajan P et al, AJOG 1999)
- Make sure cuff size is correct
  - Width of bladder 40% of circumference and encircle 80% of arm
- Correct patient position
  - Seated or semi-Fowlers
  - Quiet for 5 min
  - Feet flat on ground
  - Arm at heart level

DO NOT reposition patient on either side in order to obtain lower readings!!





Proper Blood Pressure Evaluation

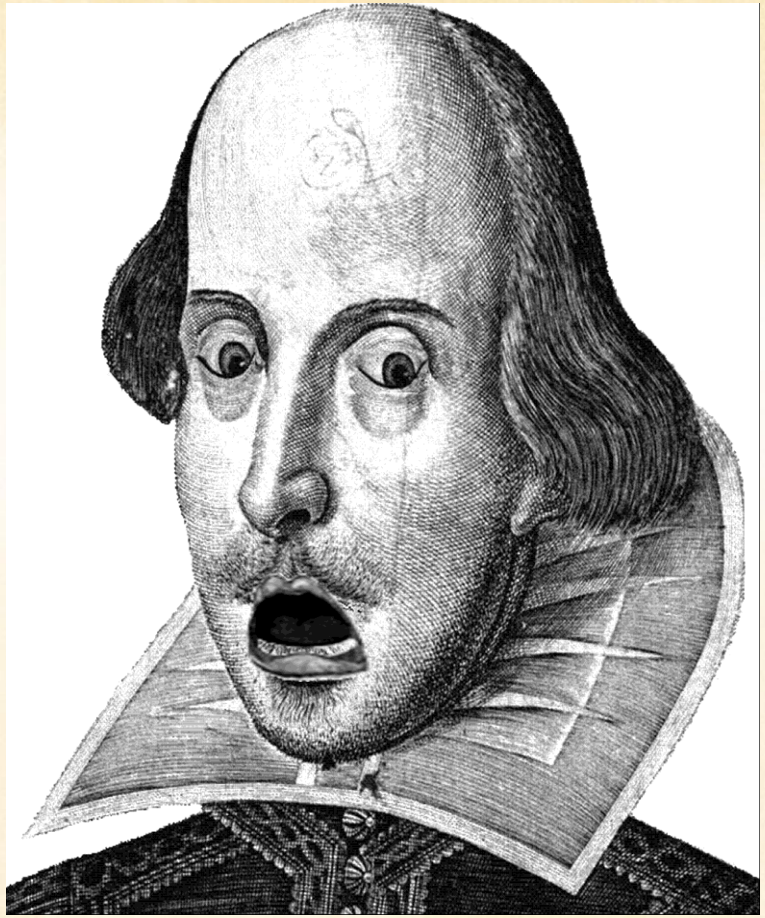
- If arm circumference is > 34 cm, large adult cuff or thigh cuff
- If arm circumference is > 50 cm, the American Heart Association recommends cuff on the forearm (although not reliable)

Initial Laboratory Workup

- **Blood work**
  - Hemoglobin/hematocrit – look for evidence of hemoconcentration or anemia
    - Hemoconcentration – intravascularly dry
    - Anemia – hemolysis
  - Platelets - <100K is severe disease
  - Liver transaminases – AST is specific to liver and hemolysis
  - Creatinine - > 1.1 is severe disease
  - LDH – hemolysis
  - Haptoglobin – if there is a concern for HELLP

Initial Laboratory Workup

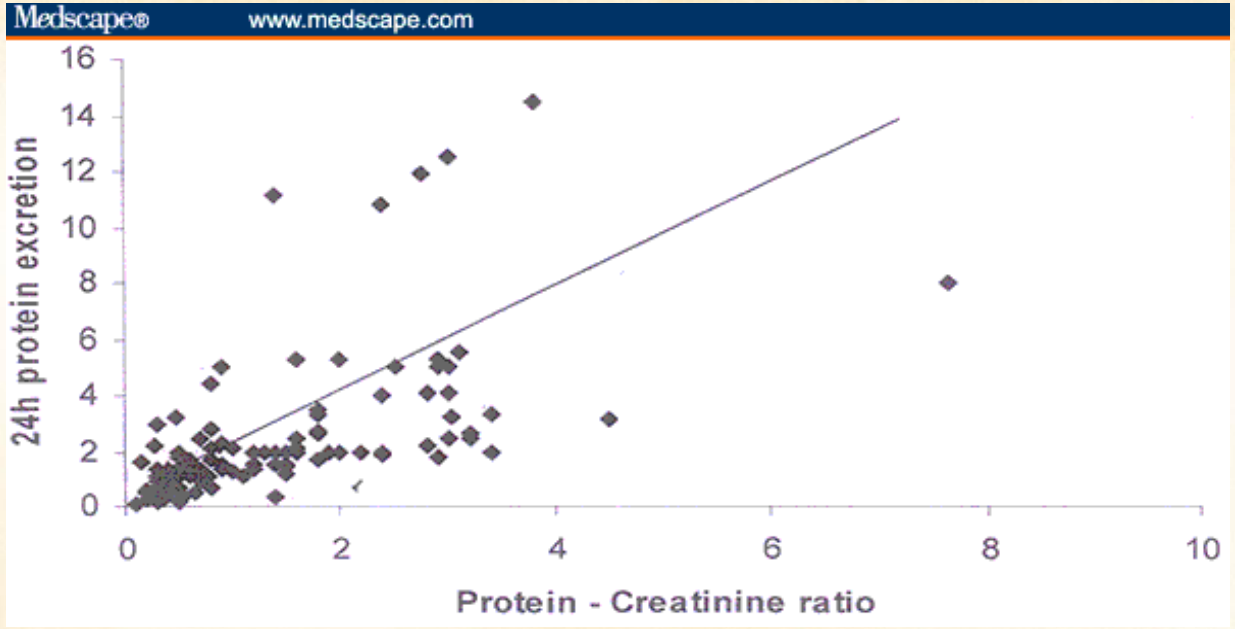
- To spill or not to spill protein…..that is the question
  - Initial workup in preeclampsia without severe features should include
    - P/C ratio (urine protein-to-creatinine ratio)
      - Different societies recommend different cutoffs
      - ACOG = ≤ 0.3 is negative
  - 24 hr urine is still gold-standard
    - Diurnal variations in protein excretion



Proteinuria Assessment

- Who should be assessed??
  - Anyone with new-onset hypertension in pregnancy

  **do not need for diagnosis in severe disease*
  - Women with underlying cHTN (differentiate exacerbation vs SIPE)
  - **No need to repeat once the diagnosis has been obtained**
    - Amount of proteinuria does not correlate with outcomes (von Dadelszen P et al., Lancet 2011)



Management

Preeclampsia without severe features

- Diagnosis made at ≥ 37 weeks
  - Delivery
    - Induction of labor
      - No increase in cesarean section risk and significant risk reduction in maternal morbidity when compared to expectant management (HYPITAT Lancet 2009)
      - Follow up economic analysis concluded induction is less costly than expectant management (HYPITAT BJOG 2010)

Preeclampsia without severe features

- Diagnosis made at ≤ 37 weeks
  - Inpatient versus outpatient management??
    - Need 24 hrs of in-patient observation to firmly establish disease severity and rate of progression
    - Compliant patient, lives close to medical center
    - Able to present at least weekly for maternal and fetal assessment
    - Able to monitor BP at home**

Out patient management of preeclampsia without severe features

- **Limited data on outcomes**
  - Observational trials comparing hospital vs out-patient management found no difference in maternal or neonatal outcomes (Dowswell T et al., Cochrane Database Sys Rev 2009)
- **Bedrest?**
  - ACOG does not recommend strict bedrest
    - Increased risk of VTE (SMFM Position Statement 2014)
  - Modified activity is acceptable
    - Can lower daily blood pressure but does not alter progression to disease

Table 2. Unadjusted and adjusted multivariate analyses for maternal outcomes, neonatal outcomes, and gestational latency

Maternal outcomes	**Unadjusted OR (95% CI)**	**Adjusted OR* (95% CI)**
SMM	**0.18 (0.06-0.59)**	0.17 (0.02-1.78)
Maternal ICU admission	**0.06 (0.01-0.56)**	0.08 (0.01-2.30)
	Linear regression coefficient (95% CI)	**Adjusted linear regression coefficient (95% CI)**
Time from diagnosis to severe features (d)	**8.84 (3.01-14.67)**	8.71 (-1.14-19.56)
Time from diagnosis to delivery (d)	**12.20 (6.60-17.81)**	-5.95 (-16.56-4.67)
Neonatal outcomes	**Unadjusted OR (95% CI)**	**Adjusted OR* (95% CI)**
5-minute Apgar score <7	0.40 (0.15-1.03)	0.33 (0.06-1.96)
Low birth weight (N=284)	**0.29 (0.15-0.57)**	0.48 (0.12-1.94)
Preterm birth	**0.24 (0.12-0.48)**	0.25 (0.06-1.06)

*Adjusted for type of HDP (gestational hypertension or preeclampsia without severe features), gestational age at HDP diagnosis, early BMI, distance from the hospital to home, maternal diabetes, and twin gestation.

Out patient management of preeclampsia without severe features

- **Medication**
  - ACOG ***does not*** recommend treatment with antihypertensive medications in women with preeclampsia without severe features or gestational hypertension
    - Mask worsening/progression of disease
    - Does not alter course of disease
  - Blood pressure should be (at the minimum) assessed twice weekly and preferably daily
  - Restriction of sodium or antidiuretics have no role in mgmt
- **Laboratory follow up**
  - ACOG recommends at least weekly lab assessment

Out patient management of preeclampsia without severe features

- **Fetal Assessment**
  - Daily fetal kick counts (10 in 2)
  - Twice weekly antenatal testing (with AFI assessment)
  - Monthly fetal growth ultrasounds
  - UA dopplers
    - Associated with 29% reduction in perinatal death with knowledge of doppler results
    - Frequency depends on results
  - If diagnosed < 34 weeks, betamethasone is recommended
  - ***Testing should be repeated when there is an abrupt change in maternal status***

- Women with co-morbidities (diabetes, lupus, etc.) or multifetal gestations should be consideration for in-patient management**
  - Atypical presentations and increased risk for worsening disease

Intrapartum management of preeclampsia without severe features

- Continuous fetal monitoring
- Strict input/output assessment
  - Risk of third spacing and pulmonary edema
  - Oliguria can be tolerated and diuretics should only be used for pulmonary edema
- Management of hypertension
  - Treat MAP of > 120-125 or persistent blood pressures ≥ 160 and/or 100 mmHg
  - Treatment does not prevent eclampsia
- Magnesium
  - ACOG does not recommend treatment of “mild” disease
  - MAGPIE trial (n=> 10,000 women)
    - NNT 100

Preeclampsia with severe features

- Diagnosed at ≥ 34 weeks
  - ACOG recommends immediate delivery

- Diagnosis at ≤ 34 weeks
  - Weigh maternal risks against fetal prematurity
  - Decision to delay
    - Odendaal HJ et al., Obstet Gynecol 1990
    - Sibai BM et al., AJOG 1994
      - Both trials found significant prolongation of pregnancy (15.4 days), significantly higher gestational age at delivery (32.9 vs 30.8 weeks), higher mean birth weights, and overall improvement in neonatal outcomes without increase in maternal morbidity

Preeclampsia with severe features

Box 4. Conditions Precluding Expectant Management

Maternal

- Uncontrolled severe-range blood pressures (persistent systolic blood pressure 160 mm Hg or more or diastolic blood pressure 110 mm Hg or more not responsive to antihypertensive medication
- Persistent headaches, refractory to treatment
- Epigastric pain or right upper pain unresponsive to repeat analgesics
- Visual disturbances, motor deficit or altered sensorium
- Stroke
- Myocardial infarction
- HELLP syndrome
- New or worsening renal dysfunction (serum creatinine greater than 1.1 mg/dL or twice baseline)
- Pulmonary edema
- Eclampsia
- Suspected acute placental abruption or vaginal bleeding in the absence of placenta previa

Fetal

- Abnormal fetal testing
- Fetal death
- Fetus without expectation for survival at the time of maternal diagnosis (eg, lethal anomaly, extreme prematurity)
- Persistent reversed end-diastolic flow in the umbilical artery

Preeclampsia with severe features: Expectant management

- Should be managed by multidisciplinary team
  - Maternal-Fetal Medicine
  - Neonatology
  - Anesthesiology
- Counseling
  - No maternal benefit, incurring risk
  - Hospitalization until delivery
  - Offered between 23/24-34 weeks

Preeclampsia with severe features: Expectant management

1. Admission to labor and delivery unit
2. Antenatal corticosteroids
   - Betamethasone
   - Dexamethasone
3. Seizure prophylaxis with magnesium sulfate
   - 4 gm or 6 gm bolus over 20 min followed by 2 gm maintenance for full 24 hrs (MAGPIE Trial)
     - NNT = 60 for severe disease
   - Does not treat blood pressures and does not prevent progression of disease
     - PROPHYLAXIS, not treatment!!
   - 5 gms per buttocks once, followed by 5 gms every 4 hrs
   - Prolonged antepartum therapy (> 5 days) has been associated with adverse effects on fetal bones

Magnesium Sulfate

- **SHOULD NOT** be considered as a blood pressure medication
- Mechanism of action
  - Decrease the permeability of the BBB and edema formation (Esen F et al., J Neurosurg Anesth 2003)
  - Raise the seizure threshold by its actions on the NMDA receptor and decrease acetylcholine in motor nerve terminals (Cotton DB et al., AJOG 1993)
- Renal excretion
  - Adjust in women with renal disease

	sBP mm Hg	sBP 30 min	sBP 120 min	dBP mm Hg	dBP 30 min	dBP 120 min
Mild Group	145 ±10	143 ±13	141 ±14	87 ±10	79 ±9	82 ±9

Belfort M, Allred J, Dildy G. Magnesium sulfate decreases cerebral perfusion pressure in

Magnesium Sulfate in the Management of Preeclampsia

Magpie Trial Collaboration Group. Do women with pre-eclampsia, and their babies, benefit from magnesium sulfate?

- 58% reduction in seizures
- 45% reduction in maternal death*
- 33% reduction in placental abruption

Serum Magnesium Concentration			
mmol/L	mEq/L	mg/dL	Effect
2–3.5	4–7	5–9	Therapeutic range
>3.5	>7	>9	Loss of patellar reflexes
>5	>10	>12	Respiratory paralysis
>12.5	>25	>30	Cardiac arrest

Altman D, Carroli G, Duley L, et al. The Magpie Trial: a randomized placebo-controlled trial; *Lancet* 2002;359:1877–90.

Recommendations for Women Who Should Be Treated With Magnesium

	Preeclampsia without severe features	Severe Preeclampsia	Eclampsia
ACOG	**	X	X
NICE		X	X
SOGC	X*	X	X
CMQCC	X*	X	X
WHO	X	X	X

***ACOG Executive Summary, 2013: for preeclampsia without severe features, it is suggested that magnesium sulfate not be administered universally for the prevention of eclampsia.*

Magnesium Toxicity Treatment

- Complications and side effects
  - Flushing, nausea, diaphoresis, vomiting, visual disturbances
  - Toxicity
    - 8.5-12 mg/dL = loss of deep tendon reflex
    - 12-16 mg/dL = respiratory paralysis
    - > 18 mg/dL = cardiac conduction abnormalities
    - > 30 mg/dL = cardiac arrest
  - Contraindicated in women with myasthenia gravis
- Treatment of toxicity
  - Calcium gluconate 1g/10ml vial given over 2-5 min

Antepartum Protocol for Management of Preeclampsia with Severe Disease

- Magnesium 24 hrs and reassess
- Symptoms assessment with vitals
- Vital signs Q 4 hrs
  - Alert physician with ANY blood pressure > 160 mmHg systolic and > 110 mmHg diastolic
- I/O every shift
- Lab assessment
  - Every other day to weekly depending on stability
- Antenatal testing
  - Daily NST
  - Once to twice weekly AFI assessment with dopplers
- Treatment with antihypertensive medications

Antepartum Protocol for Management of Preeclampsia with Severe Disease

- Prolongation of pregnancy for FETAL/NEONATAL benefit
  - 2009 systematic review of 4650 women at < 34 weeks expectantly managed
  - Pregnancy prolongation 7-14 days with maternal complication rate of < 5% (Magee et al., Hypertens Pregnancy 2009)
- Long-term outcome of children
  - The Pre-eclampsia Eclampsia Trial Amsterdam Study (PETRA)
  - 216 children born after expectant management
  - Followed at median of 4.5 years
  - Mean GA at delivery 31.4 weeks
  - Increased frequency of IQ that was subnormal (30% versus 16%)

Antepartum Protocol for Management of Preeclampsia with Severe Disease

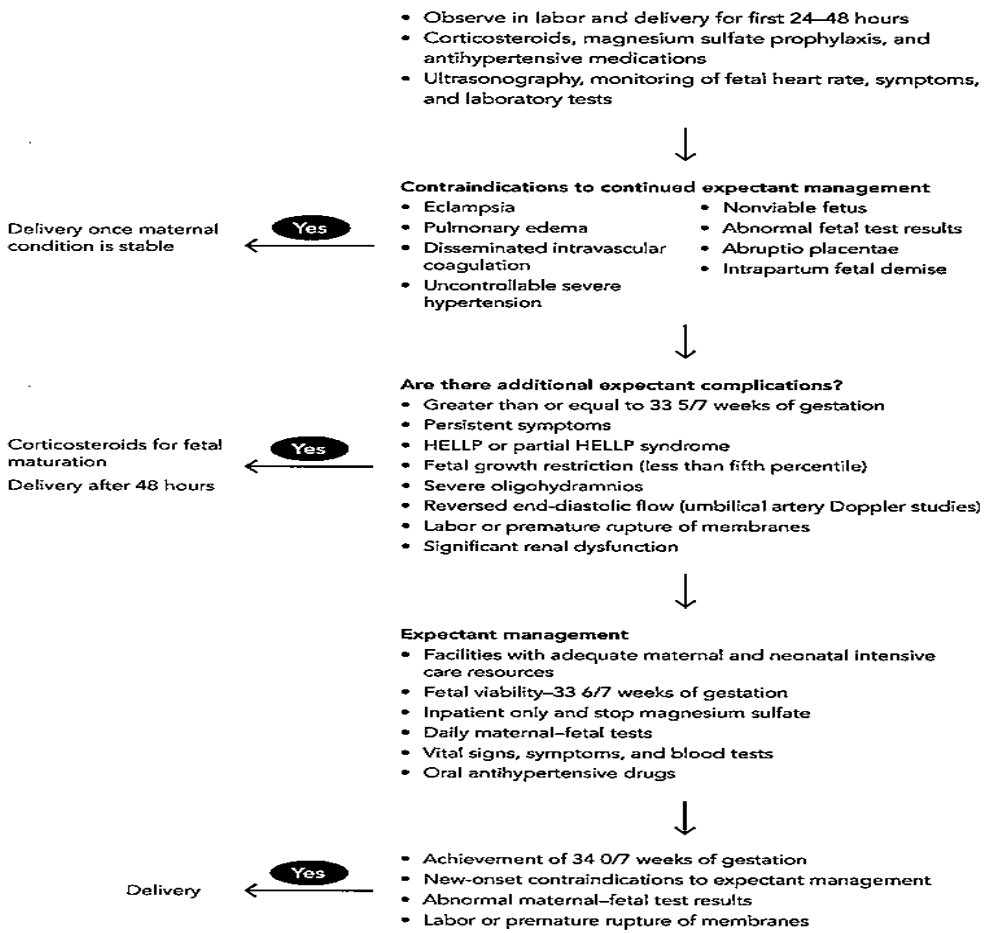


FIGURE 5-2. Management of severe preeclampsia at less than 34 weeks of gestation. ⇦
Abbreviation: HELLP, hemolysis, elevated liver enzymes, and low platelet count.

Blood Pressure Treatment Recommendations and Protocols

Preventing Stroke from Preeclampsia

Blood Pressure Comparisons: Baseline and Pre-stroke

Measure	Pregnancy Baseline (mm Hg)	Pre-stroke (mm Hg)
Mean systolic BP	110.9 ± 10.7 (n=25)	175.4 ± 9.7 (n=24)
Systolic BP range	90-136	159-198
Systolic BP % ≥ 160	0	95.8 (n=27/28)
Mean diastolic BP	67.4 ± 6.5 (n=25)	98.0 ± 9.0 (n=24)
Diastolic BP range	58-80	81-113
Diastolic BP % ≥ 110	0	12.5 (n=3)
Diastolic BP 5 ≥ 105	0	20.8 (n=5)

Antihypertensive Agents: Acute Treatment

Drug	Mechanism of Action	Dose	Onset	Max Dose	Comments
Labetalol	α and β adrenergic antagonist	10-20 mg IV, then 20-80 mg every 20 min	5-10 min	300 mg/24 hrs	Considered first line (less tachycardia); minimal side effects
Hydralazine	Arteriolar vasodilator	5 mg IV or IM, then 5-10 mg IV Q 20-40 min	10-20 min	Not to exceed 20 mg per dose	Side effects include flushing, HA, nausea
Sodium Nitroprusside	Release of NO	0.25 mg-20 mcg/kg/min IV	Within secs, half-life 2 min	Not to exceed 10 mcg/kg/min	Last resort agent; longer use assoc. with cyanide toxicity
Procardia	Calcium channel blockade, vasodilation	10-20 mg PO, repeat in 20 min then Q2-6 hrs	20 min	4 doses	Half-life 4-7 hours; 30% experience side effects (flushing, HA, dizziness)

Acute Treatment Algorithm

Evaluation and Treatment of Antepartum and Postpartum Preeclampsia/Eclampsia

Part 2: Antihypertensive Treatment Algorithm for Hypertensive Emergencies

Target BP: 130-150/80-100 mm Hg

Once BP threshold is achieved:

- Q10 min for 1 hr
- Q15 min for 1 hr
- Q30 min for 1 hr
- Q1hr for 4 hrs

*Intravenous hydralazine or labetalol should be given over 2 minutes. In the presence of sinus bradycardia or a history of asthma, hydralazine or nifedipine are preferred as initial agents. If maternal HR > 110, labetalol is preferred.

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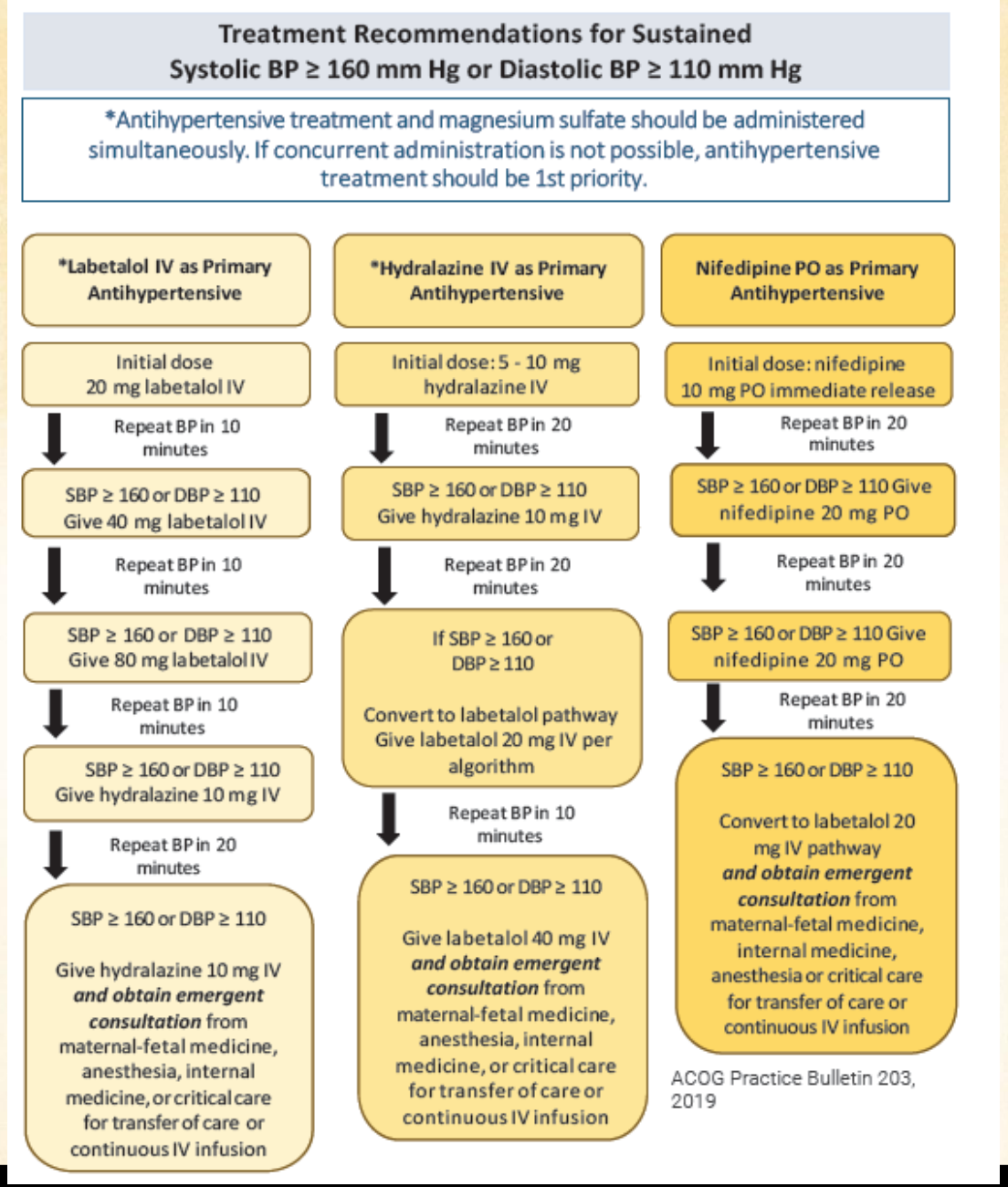

California Maternal Quality Care Collaborative. (2021, November 16). *Improving health care response to hypertensive disorders of pregnancy. A California quality improvement toolkit* [PowerPoint slides]. https://www.cmqcc.org/resources-tool-kits/toolkits/HDP

Drug Name	Mechanism of Action	Dose	MAX DOSE	COMMENTS
Methyldopa	Central acting α2-receptor agonist	500-3000 mg per day in 2-3 divided doses	3 gm/day	Available childhood safety data up to 7 yrs
Labetalol	α- and β–adrenergic antagonist	100-2400 mg daily in 2-3 divided doses	2400 mg/day	Well tolerated; associated with hypospadias in 1st trimester; bronchocontriction
Nifedipine	Calcium Channel blocker	30-120 mg per day of a slow release	120 mg/day	Do not use sublingual form
HCTZ	Thiazide diuretic	12.5 – 50 mg/day	50 mg/day	Associated with fetal demise when started in 3rd trimester; risk of intravascular depletion
Hydralazine	Vasodilation; smooth muscle relaxant	50-300 mg/day in 2-4 divided doses	300 mg/day	Rebound tachycardia when stopped; lupus-like reactions

Post Partum Management

- NSAIDS should be avoided in women with oliguria, renal failure, thrombocytopenia or poorly controlled hypertension (tend to increase blood pressure)
- Blood pressure tends to rise on PP day 3-6 (return of extravascular fluid to intravascular space) (Sibia et al., AJOG 2012)

- *“In women with gestational hypertension, preeclampsia, or superimposed preeclampsia is diagnosed, it is suggested that BP be monitored in the hospital or that equivalent outpatient surveillance be performed at least 72 hours postpartum and again 7-10 days after delivery.”*

Post Partum Management

- Uncertainty regarding level of BP to treat or target BP level
- Experts recommend treatment in the postpartum period when BP is persistently greater than 150 mmHg systolic or 100 mmHg diastolic
- Magnesium sulfate is recommended for women who present with hypertension or preeclampsia in association with severe headaches, visual changes, altered mental status, epigastric pain or SOB

Eclampsia

- New onset grand mal seizure in pregnancy
  - Eclampsia until proven otherwise!
- 2-3% of women with severe features
- 0.6% of women without severe features
- Peak incidence < 18 years and > 35 years
- Premonitory signs
  - Persistent occipital or frontal headache
  - Blurred vision
  - Photophobia
  - Epigastric or right upper quadrant pain
  - Altered mental status
- 20% of women have NO symptoms!!

Eclampsia

- 67 cases of eclampsia managed over 4 years
  - 1:310 deliveries
  - 21% had no proteinuria
  - 21% had no DBP in excess of 90 mmHg
  - 37% of first eclamptic seizures occurred postpartum
  - 16% of first eclamptic seizures occurred late postpartum (3-11 days postpartum)

***** no good predictive markers of eclampsia***

Sibai BM, McCubbin JH, Anderson GD, et al. Eclampsia. Observations from 67 Recent Cases. Obstet Gynecol; 58:609, 1981.

Eclampsia Treatment

- Key principle: maintain airway patency and prevent aspiration
  - Roll to left side
  - Prevent trauma and hypoxia
  - PREVENT RECURRENT SEIZURE
  - Treatment of hypertension
    - 20% of deaths from eclampsia
  - Evaluation for prompt delivery
- Magnesium PREVENTS seizures, it does not TREAT seizures
  - Load 4-6 gm IV followed by 1-2 gm per hour maintenance
  - Patients without IV access: 5 gm in each gluteus
  - If seizure recur (8-13%), additional 2-6 gm load over 20 min
  - No more than a total of 8 gm should be given at the outset of treatment

Eclampsia Treatment

- Treatment of seizures
  - 1-10 mg Valium
  - Slow 100 mg dose of IV thiopental sodium
  - Remember:
    - Maintain maternal airway
      - If seizures do not break – INTUBATE!
    - Prevent aspiration
    - Oxygen administration
- Neuroimaging
  - Patients with severe, unremitting headaches
  - History of CVA in pregnancy
  - Coma
  - Blindness

Prediction and Prevention

- Prediction
  - Risk stratification
  - Prior preeclampsia
    - Early onset severe disease – 9x risk
  - Maternal serum marker
    - Elevated sFlt-1 and decreased VEGF
    - 1st trimester serum markers (low PAPPA, elevated MSAFP)
    - Uterine artery dopplers
- Prevention
  - ACOG recommends daily 81 mg ASA therapy for prevention of recurrent disease in women with a history of severe or early onset disease

Long-term Maternal Risks

- Cardiovascular disease
  - Preeclampsia predictive of future cardiovascular and cerebrovascular disease up to 9 fold
  - Related to both severity and number of episodes
    - Underlying endothelial dysfunction?
    - Permanent arterial changes
  - Lifestyle interventions after preeclampsia can reduce risk by 4-13%
- Diabetes
  - Two-fold increase at 16 year follow up (Feig DS et al., PLoS Med 2013)
  - Prior preeclampsia or gHTN + DM = 16 fold increased risk

Summary

- Definitions of preeclampsia
  - Proteinuria is no longer essential to diagnosis
- Proper attainment of blood pressure is key
- Preeclampsia affects all organ systems
- Management
  - > 37 weeks delivery
  - <37 weeks without severe features – expectant mgmt
  - <34 with severe disease – expectant mgmt (maternal safety)
- Antihypertensives are an option for severe disease, not recommended for disease without severe features
- Magnesium PREVENTS seizures, does not TREAT seizures
- Should counsel women regarding future risks of prior preeclampsia

QUESTIONS??