



DIAGNOSING PREECLAMPSIA & HELLP

FLAME LECTURE: 104

BURNS/SISTO 11.15.17

LEARNING OBJECTIVES

- ▶ Classify the types of hypertension in pregnancy
- ▶ Describe the pathophysiology of preeclampsia
- ▶ List the risk factors for preeclampsia
- ▶ Recognize the signs and symptoms to diagnose preeclampsia
- ▶ See also:
 - ▶ FLAME 27 – CHRONIC HTN IN PREGNANCY
 - ▶ FLAME 105 – MANAGEMENT OF PREECLAMPSIA
 - ▶ FLAME 106 - ECLAMPSIA

DEFINITIONS

Chronic Hypertension	Gestational Hypertension	Preeclampsia w/o severe features	Preeclampsia w/ severe features	Eclampsia
Starts < 20 wks	Starts > 20 wks	Usually > 20 wks	Starts > 20 wks	Starts > 20 wks
BP > 140/90	BP > 140/90* w/ no proteinuria and no severe features	BP > 140/90* + proteinuria <i>Proteinuria defined as:</i> <ul style="list-style-type: none"> - 24-hr urine collection w/ ≥300 mg protein - P:C >0.3 - 1+ protein on urine dipstick (if other methods not avail) 	BP > 160/110* + proteinuria OR one of the following signs of end-organ damage: <ul style="list-style-type: none"> - Plt <100K - Elevated LFTs 2x normal - Cr > 1.1 or 2x normal - Pulmonary edema - New cerebral or visual symptoms 	PreE w/ or w/o severe features + Seizures (in absence of another neurological explanation for seizures)

(*on two separate occasions, 4 hours apart)

MORE DEFINITIONS!

- ▶ And this spectrum gets even more complicated...
 - ▶ **Chronic hypertension w/ superimposed preeclampsia:** when patient with known hypertension (started before the 20th week of pregnancy), develops proteinuria or signs of end-organ damage
 - ▶ **HELLP syndrome:** (Hemolysis Elevated Liver Low Platelets), often co-presents with preeclampsia but some believe it to be distinct disorder as 15-20% patients with HELLP don't have preceding HTN/pre-E²

EPIDEMIOLOGY

- ▶ Occurs in 4.6% of pregnancies worldwide (3.4% of pregnancies in United States)
 - ▶ Though definition is HTN occurring after 20 weeks, majority of cases occur later in pregnancy, later in 3rd trimester (<34 weeks)²
 - ▶ Patients with HELLP syndrome + preeclampsia, more likely to present earlier

Maternal Complications

- ▶ Women with preeclampsia are at risk for life-threatening complications of pregnancy
 - ▶ Acute kidney injury
 - ▶ Cerebral hemorrhage
 - ▶ Hepatic failure or rupture
 - ▶ Pulmonary edema
 - ▶ Disseminated intravascular coagulation
 - ▶ Progression to eclampsia

EPIDEMIOLOGY

- ▶ In US, preeclampsia is one of the top 4 leading causes of maternal death (6.4 deaths per 10,000 preeclampsia/eclampsia cases)
- ▶ Worldwide, preE/E associated w/ 10-15% of direct maternal deaths²

Pregnancy Complications

- ▶ Pregnancies complicated by preeclampsia are at risk for:
 - ▶ Placental abruption
 - ▶ Uteroplacental insufficiency
 - ▶ Increased risk of preterm delivery
 - ▶ Increased risk of cesarean section delivery
 - ▶ Oligohydramnios

PATHOPHYSIOLOGY

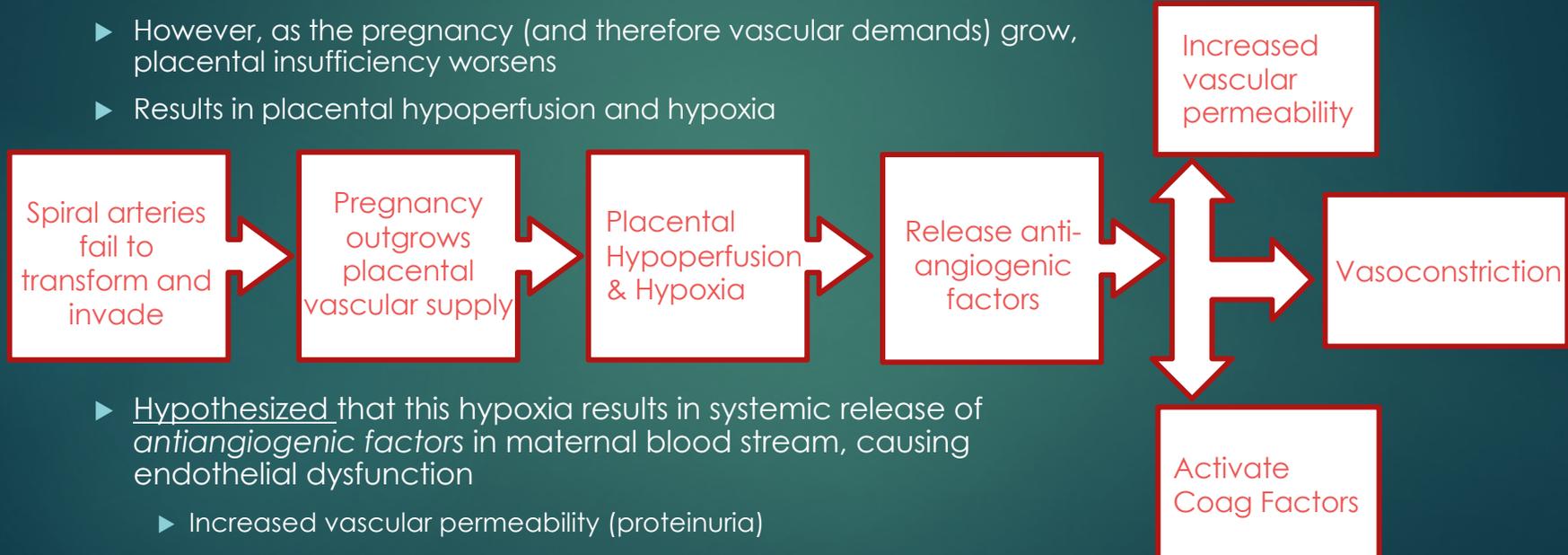
PLACENTAL ABNORMALITIES

- ▶ The pathophysiology of pre-e is still not fully solved, but we know that placenta is key:
 - ▶ Placental tissue is necessary for disease occurrence, even without fetus
 - ▶ Delivery of the placenta cures the disease
- ▶ Normally, as the placenta grows, coiled spiral arteries widen and invade myometrium to better support vascular needs of pregnancy. In pre-E:
 - ▶ Overall decreased surface area of villi (cytotrophoblasts and syncytiotrophoblasts)
 - ▶ Cytotrophoblast (CTB) invasion of the interstitial uterine compartments is shallow
 - ▶ CTBs that have invaded the uterine wall retain epithelial-like phenotypes and fail to transform to vascular-like cells
 - ▶ Spiral artery invasion is incomplete
 - ▶ Vessel abnormalities are seen (acute atherosclerosis, fibrin deposits, increased lipid-laden macrophages)

PATHOPHYSIOLOGY

PLACENTAL ABNORMALITIES

- ▶ Placental vessels show abnormalities early in pregnancy, long before clinical signs develop
 - ▶ However, as the pregnancy (and therefore vascular demands) grow, placental insufficiency worsens
 - ▶ Results in placental hypoperfusion and hypoxia



- ▶ Hypothesized that this hypoxia results in systemic release of *antiangiogenic factors* in maternal blood stream, causing endothelial dysfunction
 - ▶ Increased vascular permeability (proteinuria)
 - ▶ Vasoconstriction (hypertension)
 - ▶ Abnormal endothelial expression of procoagulants → Clinical symptoms 2/2 endothelial dysfunction at target organs

PATHOPHYSIOLOGY

IMMUNOLOGY

- ▶ It is also hypothesized that an **alloimmunologic response to paternal/fetal factors** contributes to development of preeclampsia. This is because:

PRIOR exposure to paternal and/or fetal antigens is PROTECTIVE against preeclampsia	NEW exposure to paternal/foreign antigens is correlated w/ preeclampsia
<i>Decreased risk in:</i>	<i>Increased risk in:</i>
<ul style="list-style-type: none"> ▪ Multiple pregnancies with same partner ▪ Cohabiting with partner for >1 year prior to conception 	<ul style="list-style-type: none"> ▪ Nulliparous women or women who change partners between pregnancies ▪ Women who use barrier contraception ▪ Conceive via oocyte donation or conceive via intracytoplasmic sperm injection ▪ Couples of different ethnicities

- ▶ Evidence of increased immunologic and inflammatory responses seen in placental biopsies similar to those of transplant organ rejection samples (increased NK and dendritic cells)

RISK FACTORS

Vascular disease risk factors:

- ▶ Chronic hypertension
 - ▶ Even BPs $\geq 130/80$ mmHg at initial prenatal visits
- ▶ Chronic renal disease
- ▶ Collagen vascular disease (SLE, antiphospholipid syndrome)
- ▶ Pre-gestational diabetes
- ▶ African American
- ▶ Advanced maternal age
- ▶ BMI ≥ 26

Immunologic risk factors

- ▶ History of Preeclampsia
- ▶ First pregnancy
- ▶ Family history of preeclampsia
- ▶ Multiple gestational pregnancy

*Note: **smoking** actually LOWERS risk for preeclampsia. It obviously has it's own host of complications with pregnancy but **cigarette smoking** is NOT a risk factor for preeclampsia.*



Preeclampsia Clinical Presentation

PREECLAMPSIA WORK-UP

▶ H&P

- ▶ Severe or persistent headache?
- ▶ Blurry vision, seeing black spots?
- ▶ RUQ or epigastric pain?
- ▶ Nausea/vomiting?
- ▶ Dyspnea?
- ▶ Altered mental status?

▶ Labs:

- ▶ Platelet count
- ▶ Serum Creatinine
- ▶ Serum AST and ALT

▶ Other:

- ▶ Fetal assessment (BPP or NST)
- ▶ Fetal growth scan PRN
- ▶ Labs PRN:
 - ▶ MAHA labs (LDH, bilirubin, blood smear)
 - ▶ Coag function tests (PT, PTT, fibrinogen) in setting of severe thrombocytopenia, liver dysfunction, bleeding

PRE-ECLAMPSIA DIAGNOSIS

BLOOD PRESSURE COMPONENT

Must have 2 elevated BPs \geq 4 hours apart

“MILD RANGE”

- ▶ \geq 140 mmHg Systolic or \geq 90 mmHg Diastolic

“SEVERE RANGE”

- ▶ \geq 160 mmHg Systolic or \geq 110 mmHg Diastolic

- ▶ New onset hypertension ($>$ 20 weeks of pregnancy)
 - ▶ Hypertension is earliest clinical sign of pre-e, typically worsens over time
- ▶ Extremely rarely, atypical preeclampsia can present earlier than 20 weeks, or you can have patient with chronic hypertension with superimposed preeclampsia
 - ▶ Existing hypertension + new onset proteinuria/symptoms

PRE-ECLAMPSIA DIAGNOSIS

PROTEINURIA COMPONENT

Proteinuria is defined as any of following:

- ▶ **≥ 0.3 g (300mg)** protein in 24 hr urine sample
- ▶ random **protein:creatinine ratio >0.3** in one time urine sample
- ▶ **1+ protein** on urine dipstick (if the other modalities are unavailable)

- ▶ Proteinuria is a common, but not essential finding
- ▶ Previously, "mild preeclampsia" threshold was >300mg/24hr while >5g/24hr was diagnostic for severe preeclampsia
 - ▶ However ACOG reports poor correlation between proteinuria and disease severity, thus we no longer use proteinuria for diagnosis of severe features
- ▶ Proteinuria typically worsens overtime as a result of renal damage (decreased integrity of glomerular filtration barrier and tubular damage)
 - ▶ Likely due to vasoconstriction and hypoperfusion of renal vasculature

PRE-ECLAMPSIA DIAGNOSIS

END-ORGAN DAMAGE

▶ As with proteinuria, end-organ damage is due to vasoconstriction and oxidative stress

System	Pathology	Symptom
Vascular	Endothelial damage results in capillary leakage; proteinuria causes loss of albumin	<ul style="list-style-type: none"> ▪Edema, particularly fast onset and in face, legs and lungs
Pulmonary	Inc. SVR and afterload cause pulmonary vasocongestion, worsened by hypervolemia from renal dysfunction, decreased serum albumin, and capillary damage.	<ul style="list-style-type: none"> ▪Pulmonary edema
Renal	Decreased GFR/increased plasma Cr, due to renal vasoconstriction and decreased VEGF	<ul style="list-style-type: none"> ▪Dec. urine output/Acute kidney injury ▪Hyperuricemia
Hematologic	Endothelial injury → coagulation cascade and thrombi formation in microvasculature = platelet consumption → thrombocytopenia May also have microangiopathic hemolysis	<ul style="list-style-type: none"> ▪Thrombocytopenia ▪DIC ▪Hemolytic anemia
Hepatic	Hepatic hypoperfusion leads to ischemia and hemorrhage. Endothelial dysfunction can cause HELLP syndrome. Thrombi in portal system cause swelling/necrosis of liver capsule	<ul style="list-style-type: none"> ▪RUQ pain (from capsule swelling) ▪Elevated AST, ALT
Neurological	Cerebral artery vasospasm and retinal artery spasm. Cerebral edema	<ul style="list-style-type: none"> ▪Headache ▪Blurry vision ▪Hemorrhagic stroke ▪Seizures (= eclampsia)

PRE-ECLAMPSIA DIAGNOSIS

TRICKY IN PATIENTS WITH CHRONIC HTN

- ▶ Women with chronic HTN may already have baseline proteinuria
 - ▶ Thus, while you cannot make a diagnosis using proteinuria, you can compare their current proteinuria to their baseline (hopefully collected earlier in pregnancy) to look for acute rises
- ▶ Women with chronic HTN will have a steady elevation in both their systolic and diastolic BPs from 20 weeks until delivery
 - ▶ Thus, practitioners need to have a high index of suspicion for superimposed pre-eclampsia before titrating up home blood pressure meds
- ▶ Likely new neurologic symptoms or abnormal Cr/LFTs may be the most specific indicators, however, blood pressures that have dramatically increased over baseline or are not responding adequately to IV anti-hypertensives are also clues

DIAGNOSTIC REVIEW¹

- ▶ New onset hypertension + proteinuria AND/OR end-organ damage in previously normotensive woman

Blood Pressure

Systolic BP ≥ 140 mmHg
AND/OR
Diastolic BP ≥ 90 mmHg

+

Proteinuria

≥ 300 mg/24hr urine
AND/OR
Protein:creatinine ≥ 0.3

OR

End Organ Dysfunction

Platelets < 100 k/ μ L
AND/OR
Serum Cr > 1.1 mg/dL (or
2x baseline)
AND/OR
Elevated LFTs (2x normal)
AND/OR
Cerebral/visual Sx
AND/OR
Pulmonary Edema

HELLP SYNDROME

- ▶ Hemolysis, Elevated Liver, Low Platelets
- ▶ Most often occurs in conjunction with preeclampsia, but 1/5 of patients with HELLP don't have preceding diagnosis of preeclampsia
- ▶ Labs show *schistocytes* on blood smear, *elevated LDH* and *indirect bilirubin*, *decreased hemoglobin*
- ▶ Risk of developing DIC

Distinguishing syndromes with ↑ LFTS:

HELLP	↑ LDH, Bilirubin + <u>hemolysis</u> , ↓ Plt
AFLP*	↑ <u>Ammonia</u> , ↓ Glucose, Fibrinogen
ICP**	↑ <u>Bile acids</u> , (symptoms: itching palms and soles)

*AFLP: Acute Fatty Liver of Pregnancy

**ICP: Intrahepatic Cholestasis of Pregnancy



REFERENCES & RESOURCES

- ▶ Hypertension in Pregnancy: Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. *Obstet Gynecol*, Nov 2013; 122(5):1122-1131.
- ▶ UpToDate – Preeclampsia: Clinical features and diagnosis
- ▶ Uzan J, Carbonnel M, Piconne O, Asmar R, Ayoubi J-M. Preeclampsia: pathophysiology, diagnosis, and management. *Vascular Health and Risk Management*. 2011;7:467-474 doi:10.2147/VHRM.S20181.
- ▶ Callahan, Tamara L., and Aaron B. Caughey. *Blueprints Obstetrics & Gynecology*. Philadelphia: Wolters Kluwer Health/Lippincott William & Wilkins, 2009. 6th ed.