

Pregnancy-Related Cardiac Conditions – Just a Pregnant Pause?

Hypertensive disorders of pregnancy, including gestational hypertension, pre-eclampsia and the HELLP syndrome affect up to 10% of American women, and are a predisposing factor for the development of peripartum cardiomyopathy. Though manifestations of these disorders often improve in the post-partum period, there are long-term health implications to consider in the underwriting process.



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Pregnancy-Related Cardiac Conditions

Just a Pregnant Pause?

Valerie R. Kaufman, MD, FACC, DBIM

01.23.2023

Outline

- Hypertensive disorders of pregnancy
- Adverse pregnancy outcomes
- Peripartum cardiomyopathy
- Short and long term effects





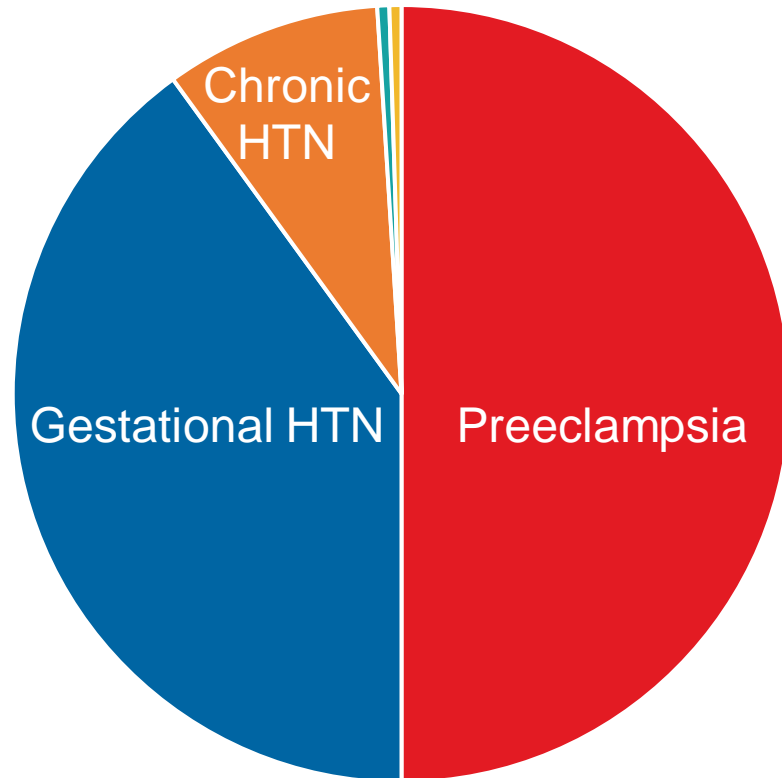
Hypertensive Disorders of Pregnancy

Discussion Questions: Hypertensive Disorders of Pregnancy

1. What are the hypertensive disorders of pregnancy?
2. What causes these conditions in some women but not others?
3. Are there risk factors?
4. What short term risks are associated with HDP?
5. Do these conditions resolve with the end of pregnancy/childbirth?
6. Are there long term risks?



Hypertensive Disorders of Pregnancy (HDP)



- Preeclampsia
- Gestational HTN
- Chronic HTN
- Preeclampsia and HTN
- Eclampsia

- Leading cause of maternal and fetal morbidity and mortality
- Associated with up to 30% of maternal deaths in US
- Incidence is rising –10-15% experience hypertensive pregnancy
- Most studies are relatively short term
- 5-fold risk of developing chronic HTN
- 2-fold risk of other CVD including
 - Stroke
 - CAD
 - Heart failure
 - Arrhythmias
 - CKD
 - Valvular disease
- Long-term changes in child exposed in utero

Case Studies: Hypertensive Disorders of Pregnancy

Case Study 1A: Near Term Risk

- 32 year old woman
 - Overweight, otherwise good health
 - Had preeclampsia with first pregnancy, induced at 38 weeks (3 years ago)
 - Currently 24 weeks pregnant
 - BP on exam 126/80
 - Urinalysis negative
- *Would you postpone until delivery?*
- *How would you assess after delivery?*

Case Study 1B: Longer Term Risk

- 45 year old woman
 - C/S at 34 weeks 10 years ago
 - C/S 6 years ago, complicated by HELLP syndrome
 - Fully recovered, not on any meds
 - Does not plan to have any more children
 - Only follows up with OB/GYN
 - Overweight, BP on exam 140/86
- *How would you assess at this time?*

Gestational Hypertension

**Systolic BP \geq 140
OR
Diastolic BP \geq 90**

~~Onset after
20 weeks
gestation~~

~~Resolved by
12 weeks
postpartum~~

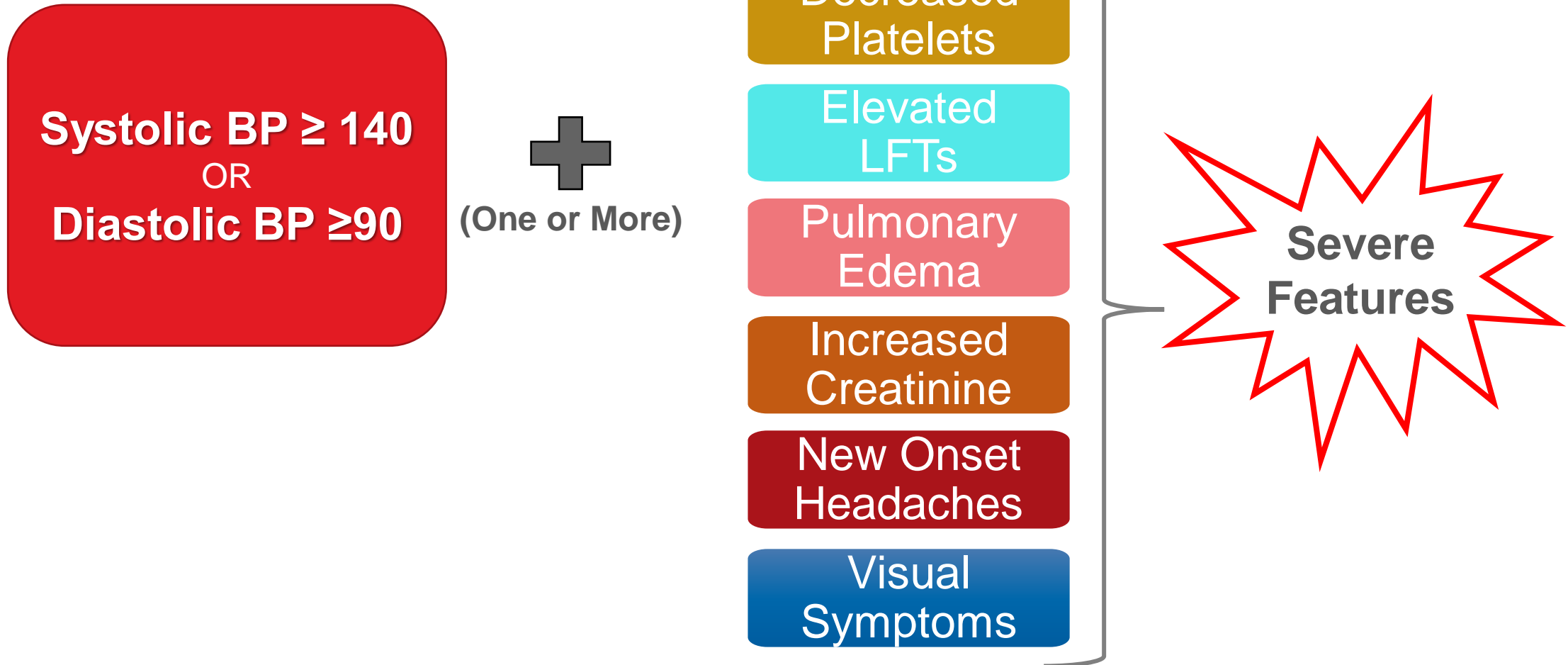


~~No
proteinuria or
end organ
dysfunction~~

*Chronic
HTN*
5X

Preeclampsia
10-25%

Preeclampsia



Risk Factors for Preeclampsia

Obstetrical

- First pregnancy
- Preeclampsia in prior pregnancy
- Adverse pregnancy outcome
- Maternal age >40 (? < 18)
- Multifetal gestation
- Assisted reproductive technologies
- FH of preeclampsia
- Male partner factors

Other

- Obesity
- Preexisting HTN
- DM, either preexisting or gestational
- Chronic kidney disease
- Vascular disease



Preeclampsia

- Multisystem and progressive
- Acute process ends when pregnancy ends
- Incidence is increasing
 - About 5% of first pregnancies
 - 5% of subsequent pregnancies
- Risks for both mother and infant



	Near Term Risks	Long Term Risks
Mother	<ul style="list-style-type: none">• Placental abruption• Progression to eclampsia• Death (<0.1%)• Increased risk of HDP and PPCM with future pregnancy	<ul style="list-style-type: none">• HTN• CAD• Arrhythmias• Heart failure• Valvular heart disease• CKD
Infant/Child	<ul style="list-style-type: none">• Pre-term delivery• Small for gestational age• Stillbirth• Placental abruption	<ul style="list-style-type: none">• Increased BP• Increased BMI

Subtypes of Preeclampsia

- Late onset - > 34 weeks gestation
- Early onset - \leq 34 weeks gestation
- Preeclampsia with severe features – includes severe HTN
- HELLP syndrome
 - Hemolysis, elevated liver enzymes and low platelets
 - Usually has HTN and proteinuria but rarely does not
- Eclampsia – seizures along with other features of preeclampsia
 - Complications in 70%
 - Maternal mortality rate up to 1.8%
 - Risk of preterm birth – 5-7x increased
 - Fetal mortality increased

Severe HTN

Decreased Platelets

Elevated LFTs

Pulmonary Edema

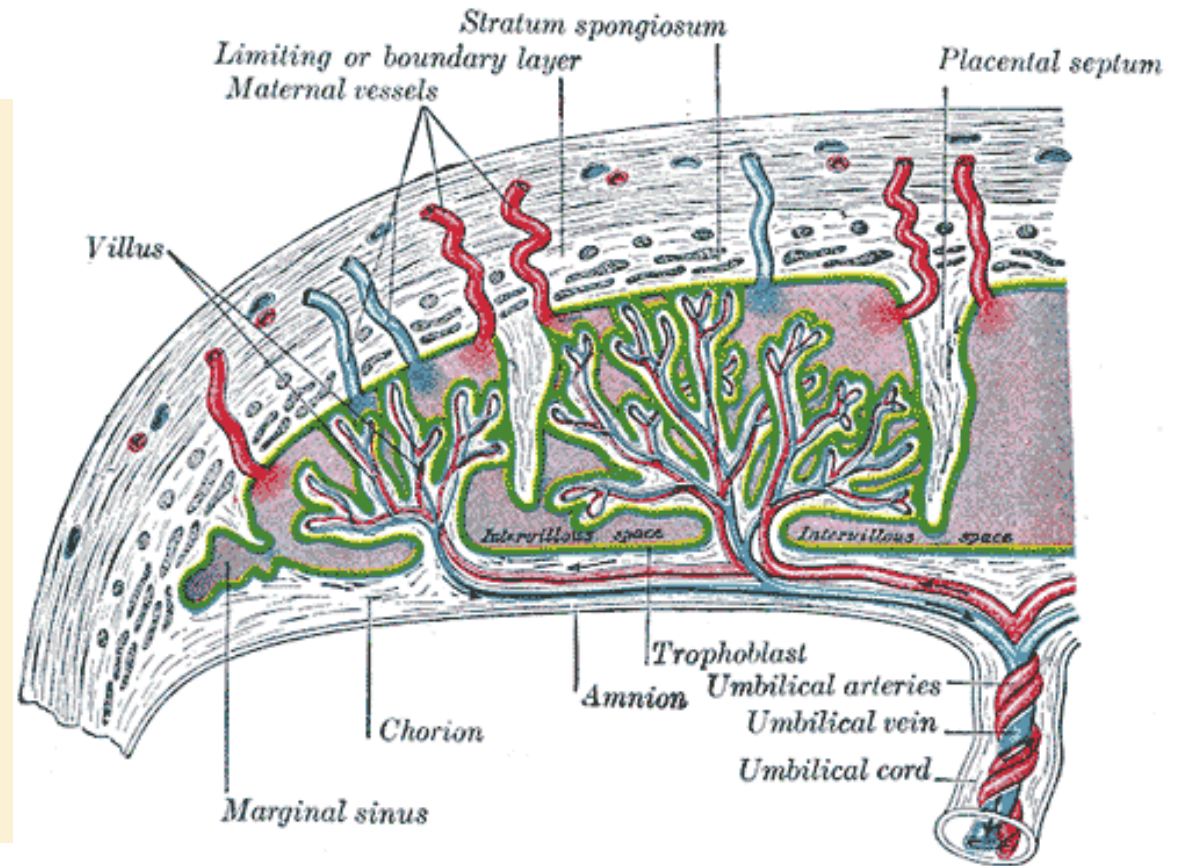
Increased Creatinine

New Onset Headaches

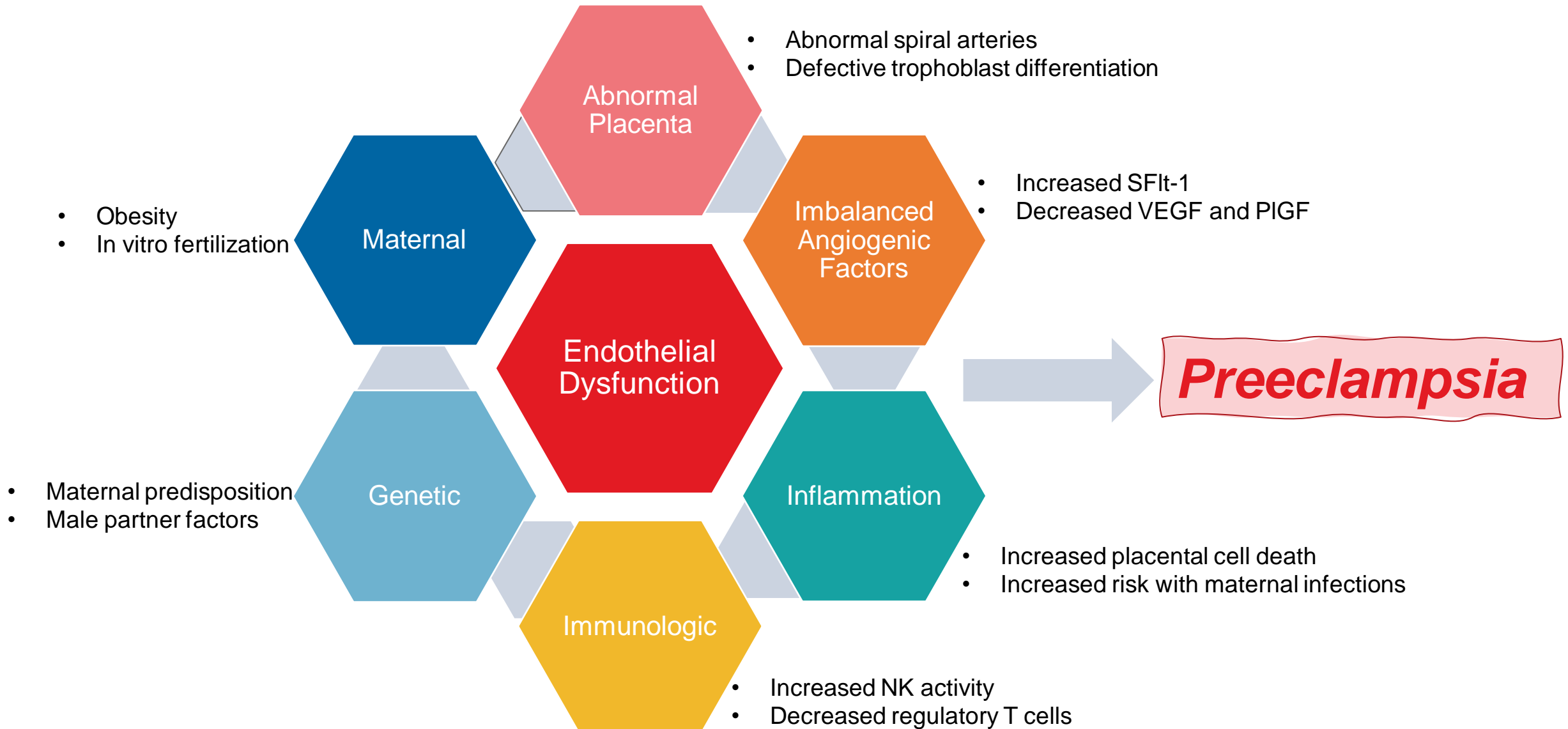
Visual Symptoms

Preeclampsia and the Placenta

- Not completely understood
- Multiple factors lead to abnormal placental development
- Placental underperfusion leads to release of antiangiogenic factors into maternal circulation
- Inflammatory and immune factors activated
- Systemic endothelial dysfunction results
- Trigger for this cascade not known



Pathogenesis of Preeclampsia



Long-Term Cardiovascular Risk After Hypertensive Pregnancy

- Large prospective, observational study based on UK Biobank
- 220,024 women, 2808 had hypertensive disorder of pregnancy
- Mean age at baseline: 57
- Followed for 7 years: 7.0 (HDP) vs 5.3 (no HDP) incident CVD diagnoses per 1000 women-yrs

Condition	Hazard Ratio	CI	P-Value
Mitral regurg	5.0*	1.5-17.1	0.01
Aortic stenosis	2.9*	1.5-5.4	< 0.001
CAD	1.8	1.2-2.6	< 0.001
Heart failure	1.7	1.04-2.6	0.03

**Absolute risk is small*

- Some but not all increased risk associated with prevalent HTN
- SFlt-1 (soluble fms-like tyrosine kinase-1) – antiangiogenic protein associated with preeclampsia and calcific AS

Hypertensive Disorders of Pregnancy: Risk Assessment

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Hypertensive Disorders of Pregnancy: Risk Assessment

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 - Urinalysis negative
- *Would you postpone until delivery?*
 - *Some risk of recurrence, but low*
 - *Low risk of severe complications*
 - *Otherwise in good health*
 - *Regular OB care?*
- *How would you assess after delivery?*
 - *If no HDP with 2nd pregnancy, more favorable*
 - *If HDP with 2nd pregnancy, some increased long term risk (as for multiple CV risk factors?)*

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 - Only follows up with OB/GYN
 - Overweight, BP on exam 140/86
- *How would you assess at this time?*
 - *Overweight with current increased BP*
 - *Increased risk for other cardiovascular diseases*
 - *Review carefully for evidence of other CV disease or complications of HTN*

Adverse Pregnancy Outcomes

- Include
 - Spontaneous pre-term birth
 - Intrauterine growth restriction
- Common: 10-20% of pregnancies
- Increasing in frequency. Significant racial disparities
- Likely shared pathogenic factors with hypertensive disorders of pregnancy
 - Defective placentation
 - Pro-inflammatory state
 - Production of anti-angiogenic proteins (sFlt-1)
 - Vascular dysfunction such as increased arterial stiffness, endothelial and myocardial dysfunction



Adverse Pregnancy Outcomes and Long Term Risk

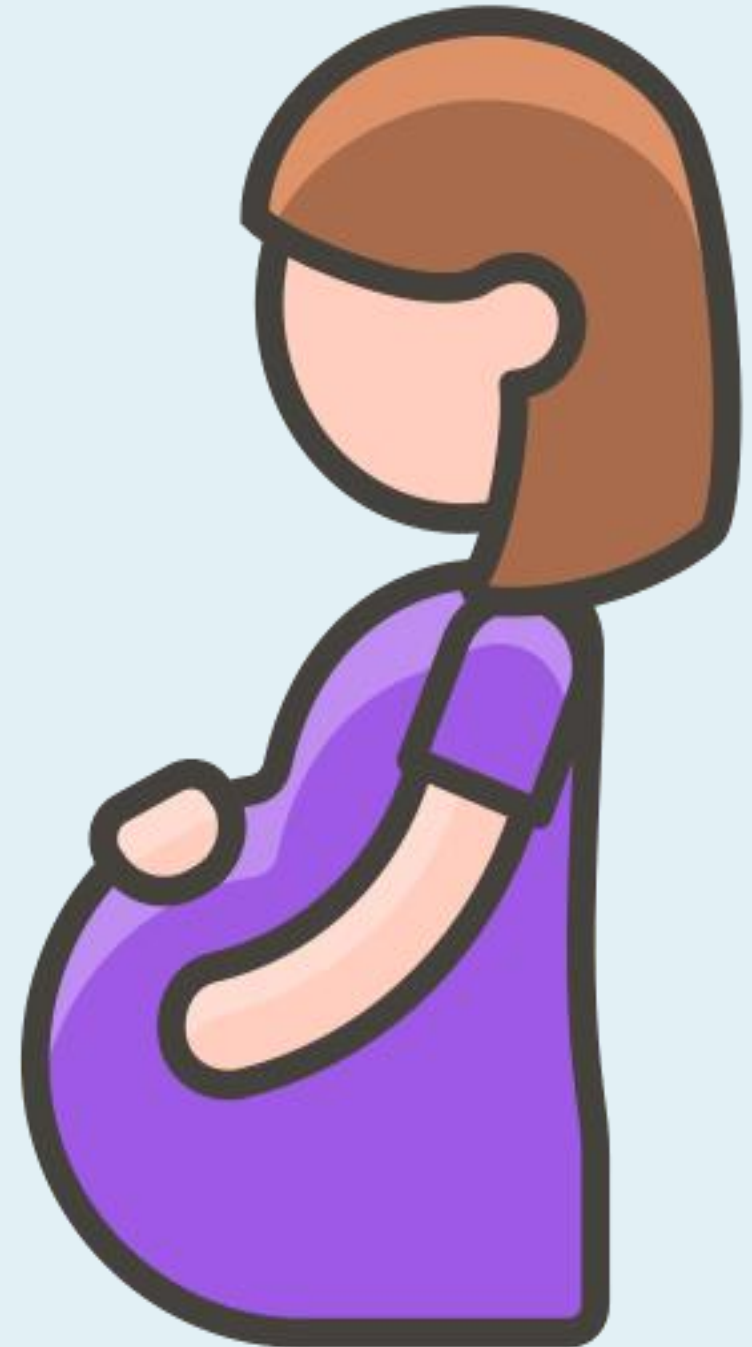
- Increased risk of hypertensive disorders with subsequent pregnancies
- Increased risk of peripartum cardiomyopathy with subsequent pregnancies
- Increased risk of future CVD such as HTN, CAD, heart failure and possibly stroke
 - Endothelial dysfunction and diastolic dysfunction similar to what occurs in Heart Failure with Preserved EF (HFpEF)
 - Higher central arterial stiffness
 - Higher Carotid Intimal Medial Thickness (CIMT)
 - Aberrant sympathetic neural activity and cardiac response (inability to increase stroke volume)
- Increased risk of renal disease



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Peripartum Cardiomyopathy



Case Study #2

- 37 year old woman, nonsmoker
- 5'5" (165 cm), 216 lbs (98.1 kg), BMI 35.9
- Complicated obstetrical history
 - Miscarriage 2014
 - Uncomplicated pregnancy 2016
 - Pre-eclampsia leading to induction at 38 weeks in 2018
 - Episode of heart failure at delivery in 2020, full recovery
 - Currently pregnant, 14 weeks at time of application

What else would you want to know?



- Details about heart failure episode
- Chronic HTN?
- Most recent echo
- Family history
- Regular follow up?

Case Study #2: Additional Information

- Considered “high risk” due to complicated OB history and advanced maternal age
- Regular OB follow up
 - Single fetus
 - No cardiac symptoms noted
 - BPs normal
- Had pulmonary edema following last delivery in 2020 – thought to be due to volume overload
 - Initial echo: LV mildly dilated at 5.8 cm (*normal up to 5.4 cm*), EF 45%
 - Echo at 3 month follow up: LV 5.5 cm, EF 52%
 - No further cardiac follow up



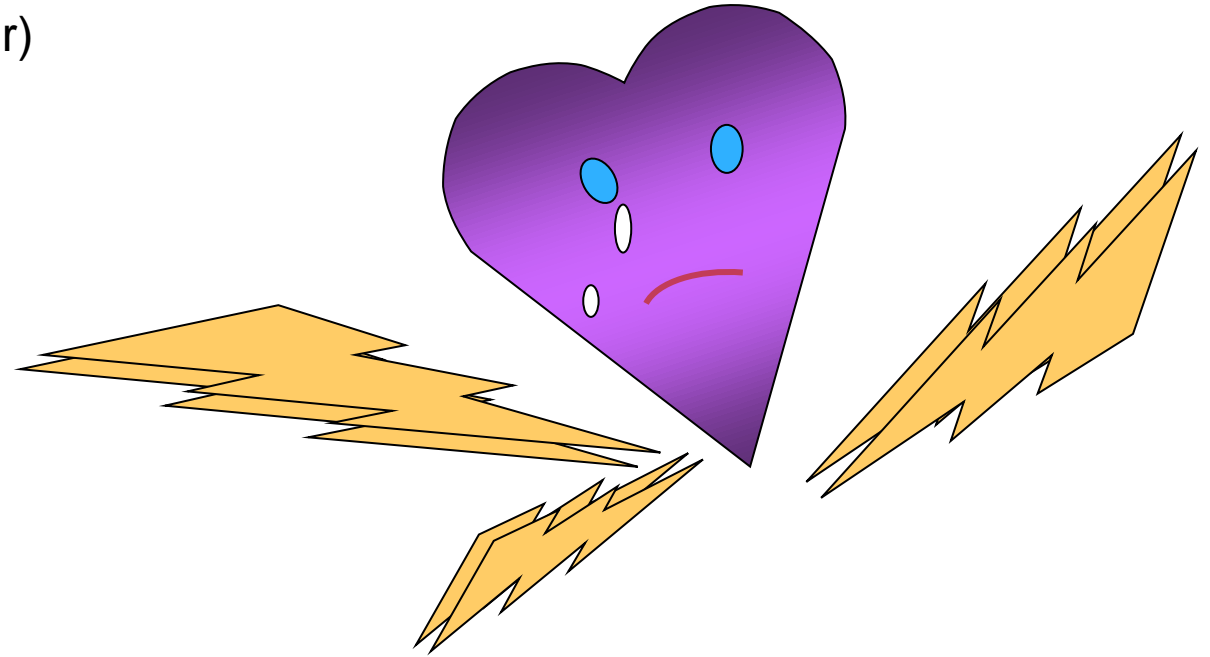
Discussion Questions: Peripartum Cardiomyopathy

1. What are possible reasons for heart failure associated with pregnancy?
2. What is peripartum cardiomyopathy?
3. Is there a connection between hypertensive disorders of pregnancy, adverse pregnancy outcomes and peripartum cardiomyopathy?
4. Is there a risk of recurrence with peripartum cardiomyopathy?
5. Are there long-term risks with peripartum cardiomyopathy?



Possible Causes of Heart Failure During Pregnancy

- Underlying heart disease
 - Cardiomyopathy (dilated, hypertrophic or other)
 - Congenital Heart Disease
 - Valvular Heart Disease
 - Hypertensive Heart Disease
 - CAD
 - Left ventricular noncompaction
- Preeclampsia
- Peripartum cardiomyopathy
- Takotsubo cardiomyopathy
- Myocarditis
- Pulmonary embolism
- Iatrogenic – such as volume overload



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Peripartum Cardiomyopathy (PPCM)

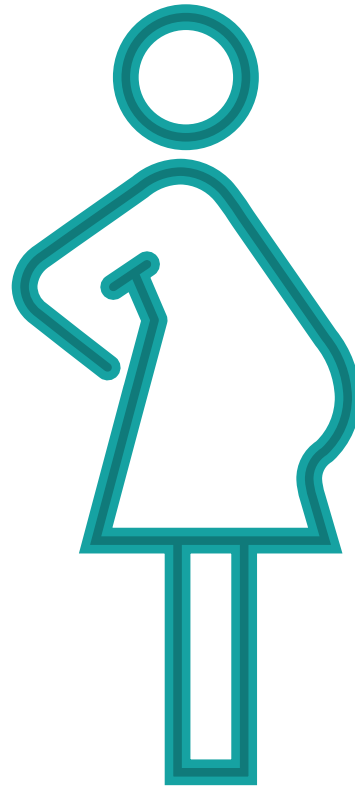
Definition: *Idiopathic LV systolic dysfunction that develops during pregnancy or in the early postpartum period*

■ Incidence

- US: 1:1000 to 1:4000
- Haiti: 1:300
- Japan: 1:20,000

■ Risk factors

- Maternal age > 30
- African descent
- Pregnancy-related HTN
- Multiple fetuses
- Multiparity

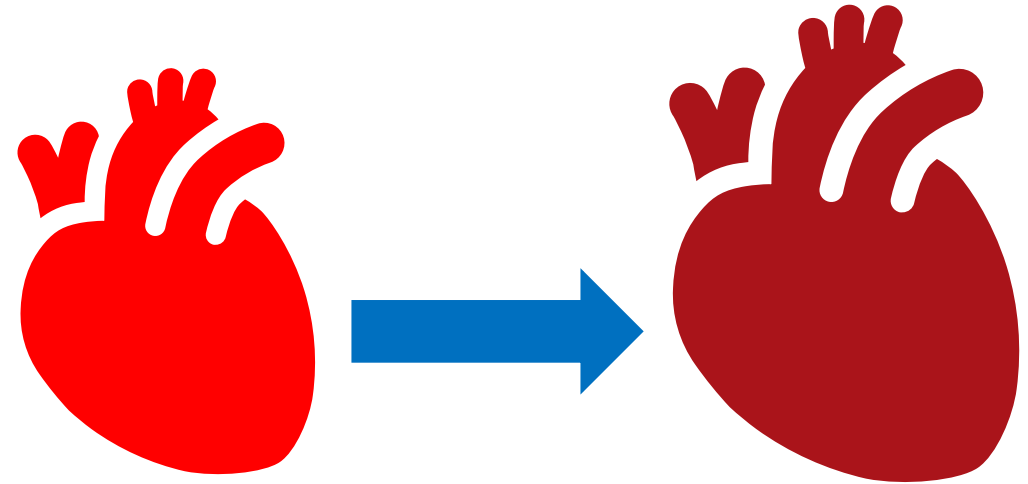


■ Potential Causes

- Pregnancy-related hemodynamic changes
 - Immunologic factors
 - Myocarditis
 - Altered prolactin processing
 - Angiogenic/vasculohormonal imbalance
 - Genetic predisposition
- Typically diagnosed after delivery within the first month postpartum

Dilated (Nonischemic) Cardiomyopathy

- Characterized by
 - LV dilatation
 - Impaired systolic function
- Common causes
 - Genetic (25-50%)
 - Post-inflammatory or post-infectious
 - Drugs (cocaine, chemotherapeutic agents, trastuzumab)
 - Toxins (alcohol)
 - Mediastinal radiation
 - Pregnancy (peripartum cardiomyopathy)
 - Prolonged tachyarrhythmias (tachycardia-mediated cardiomyopathy)
- Most are progressive although some may be reversible



PPCM - Prognosis

Caveat: Studies are small

Acute Complications

- Major adverse event precedes diagnosis in about half of cases
- Short term complications
 - Heart failure
 - Arrhythmias
 - Thromboembolic events
 - Stroke
 - Death
- Mortality 4-11% at 1 year
- “Majority” show partial or complete recovery within 2-6 months

Chronic/Long Term Concerns

- Prognostic markers
 - EF at time of diagnosis (< 30% is unfavorable)
 - LV dilatation
 - LV thrombus
 - RV systolic dysfunction
 - Recovery EF < 50%
- Subsequent pregnancy
 - Worsening of LV function in about 1/3
 - Fully recovered: 20% risk of recurrence
 - EF < 50%: 50% have further deterioration
 - Mortality 2% - 19%
 - Increased risk of prematurity and miscarriage
- Long-term mortality 7-20% (over 8 years)

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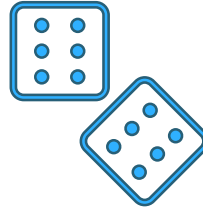
What would your recommendation be at this time?

What if she wasn't currently pregnant?

If she was now age 55 and asymptomatic. Concerns?

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What would your recommendation be at this time?

- *Significant risk of recurrent PPCM*
- *Chance of worse outcome with recurrence*
- *High risk*

What if she wasn't currently pregnant?

- *At risk for recurrent PPCM with subsequent pregnancies*
- *Chance of worse outcome with recurrence*
- *High risk*

If she was now age 55 and asymptomatic. Concerns?

- *At increased risk for multiple CV impairments*
- *Would be concerned about current cardiac status and assess carefully*
- *With good follow up, would consider as nonischemic cardiomyopathy*

Short and Long Term Risks: Summary

	Short Term	Long Term
Adverse Pregnancy Outcomes Preterm delivery Intrauterine growth restriction	<ul style="list-style-type: none"> Placental abruption Risk to fetus 	<ul style="list-style-type: none"> ↑ maternal risk of HDP and PPCM ↑ maternal risk of CVD and CKD
Hypertensive Disorders Gestational HTN Preeclampsia	<ul style="list-style-type: none"> Placental abruption Mortality <0.1% with preeclampsia Progression to eclampsia (mortality 1.8%) ↑ risk of HDP and PPCM with future pregnancy Risk to fetus (including stillbirth) 	<ul style="list-style-type: none"> With subsequent pregnancy <ul style="list-style-type: none"> ↑ maternal risk of recurrent HDP ↑ maternal risk of PPCM 5x ↑ maternal risk of chronic HTN 2x ↑ maternal risk of CVD ↑ maternal risk of CKD ↑ BMI and BP in children
Peripartum Cardiomyopathy	<ul style="list-style-type: none"> Heart failure Arrhythmias Stroke 4-11% one-year mortality 	<ul style="list-style-type: none"> With subsequent pregnancy <ul style="list-style-type: none"> 1/3 have deterioration in LV function 2-19% mortality ↑ risk of preterm birth and fetal loss Long term mortality 7-20% ↑ maternal risk of CVD

Key Takeaways

- The most common HDP are gestational hypertension and preeclampsia
- High risk markers for preeclampsia include
 - Other-than-first pregnancy
 - Early onset (before 34 weeks gestation)
 - Severe features
 - Underlying heart disease or other medical conditions
- Long term maternal risks following HDP include increased risk of HTN, CAD, valvular disease and heart failure
- Children born of hypertensive pregnancies have higher BP and BMIs
- Most but not all cases of PPCM improve within 6 months postpartum
- After PPCM, LV function deteriorates in 20-50% with subsequent pregnancies



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