MATERNAL911®






Hypertensive Disorders of Pregnancy

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Course Description:

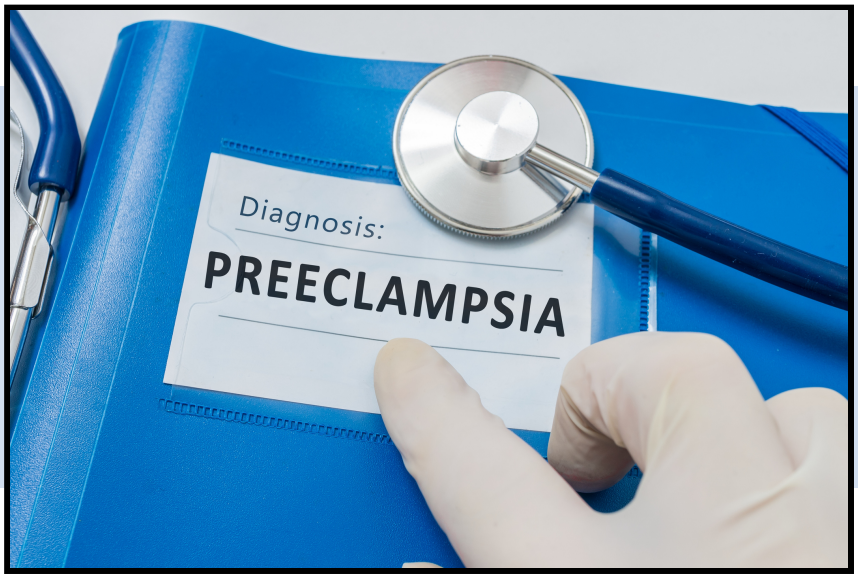
Hypertensive disorders in pregnancy remain one of the leading causes of maternal death. The Maternal 911 Severe Preeclampsia module will give you a basis of knowledge to better recognize and treat preeclampsia. This knowledge base will help with communication to the patient and her family. The goal would be to increase the maternal safety for the unit where she will undergo care and delivery.

Approximate Time to Complete: 120 minutes

Click here to download a print version of this course.

The purpose of this module is for the participant to:

- Explain criteria for preeclampsia, severe preeclampsia, and eclampsia.
- Identify risks associated with causing preeclampsia.
- Recognize the signs and symptoms of worsening preeclampsia so prompt health care delivery can be implemented.
- Describe the pathogenesis of preeclampsia.
- Identify clinical features and pathophysiology by organ system.
- Describe the medications used for resuscitation and how they may affect the woman and expected outcomes.



Preeclampsia is a multi-system progressive disorder characterized by new onset hypertension and proteinuria, or hypertension and end-organ dysfunction with or without proteinuria, in the last half of pregnancy or postpartum, often in a previously normotensive woman.

Diagnosis of Pre-eclampsia

Preeclampsia is defined as systolic blood pressure (BP) > 140 mmHg or diastolic BP > 90 mmHg on two occasions, at least four hours apart, after 20 weeks of gestation in previously normotensive woman with proteinuria >0.3 grams in a 24-hour urine specimen or protein(mg/dL)/creatinine (mg/dL) ratio > 0.3.

Preeclampsia with severe features

Diagnosis of Gestational Hypertension

Defined as a systolic blood pressure of 140 mmHg or more or a diastolic blood pressure of 90 mmHg or more, or both, on two occasions at least 4 hours apart after 20 weeks gestation in a woman with previously normal blood pressure.

Diagnosis of HELLP Syndrome

- HELLP is abbreviation for Hemolysis, Elevated Liver enzymes and Low Platelet count syndrome.
- Hemolysis
  - LDH >600 IU/L
- Elevated Liver Enzymes
  - AST, ALT > 2x the upper limit of normal
- Low Platelets
  - Platelets <100,000
- Does not require the presence of hypertension or proteinuria
- 30% of cases present or worsen postpartum

Diagnosis of Pre-eclampsia with Severe Features

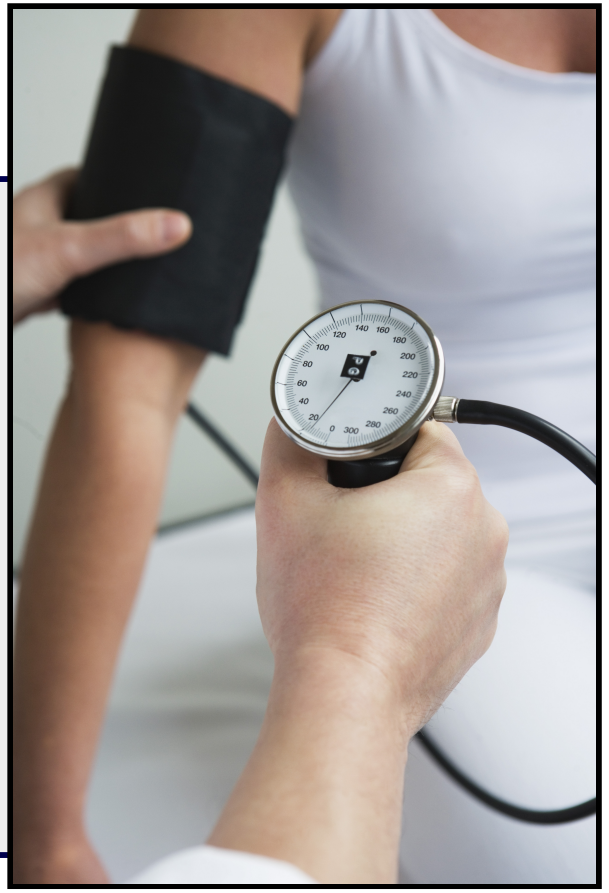
Hypertension

- New onset systolic blood pressure of 160 mmHg or more, or diastolic blood pressure of 110 mmHg or more
- Treatment of severe range BP should not be withheld for the purposes of diagnosis

Pre-eclampsia with severe features should be diagnosed in any patient with gestational hypertension in conjunction with any of the following:

Lab abnormalities

- Thrombocytopenia
  - Platelet count <100,000
- Impaired liver function with no alternative etiology
  - 2x the upper limit of normal or persistent right upper quadrant or epigastric pain unresponsive to medication



Diagnosis of Pre-eclampsia with Severe Features

Renal insufficiency

- Creatinine >1.1 mm/dL or doubling of a baseline creatinine in the absence of other renal disease

Pulmonary edema

- Maternal symptoms
  - New onset headache unresponsive to medication and not accounted for by alternative diagnoses
  - New onset visual disturbances

Pre-eclampsia with severe features does not require proteinuria

It is important to note the collection of 24 hour urine should not delay treatment.

The protein creatinine ratio is calculated with this formula:
(urine protein x 0.88) + (urine creatinine)

An online calculator can be found at:
https://www.easycalculation.com/medical/urinaryprotein.php

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Urinary Proteins Excretion C

easycalculation.com

Urine Protein	
Urine Creatinine	
Uprot / Ucreat	
Estimated 24 hour urine protein	

Eclampsia is diagnosed when grand mal seizures occur in a woman with no history of neurological conditions and evidence of hypertension or other evidence of preeclampsia.

Seizures can occur before, during, or after delivery of the fetus.

Preeclampsia

- Complicates 2-8% of pregnancies worldwide [1].
- The prevalence of preeclampsia in the United States (U.S.) is about 3.4% but 1.5- to 2-fold higher in first pregnancies [2].

Click the above arrows to see more information.

Eclampsia

- Occurs in 2 to 3% of women with severe features not receiving anti-seizure prophylaxis and up to 0.6% of women with preeclampsia without severe features [3].
- The incidence of eclampsia has been stable at 1.6-10 cases per 10,000 deliveries in developed countries [4-9].

Click the above arrows to see more information.

Hypertensive complications of pregnancy is 1 of the 3 leading causes of maternal death in the United States [12-14].

Approximately one maternal death per 100,000 live births is due to preeclampsia or eclampsia with a case fatality rate of 6.4 deaths in 10,000 cases [15-17].

It is imperative to educate women during their pregnancy regarding the signs and symptoms of preeclampsia and empower her to reach out for help if these occur.

Click the above arrows to see more information.

Pathophysiology of Preeclampsia

Maternal and fetal placental factors are involved in the pathophysiology of preeclampsia with both affecting the severity of the disease.

Studies on placental pathology have demonstrated that preeclampsia is associated with abnormal uterine spiral artery remodeling and trophoblastic invasion, but the cause of this remains unknown [23,24].

It has been found that the spiral artery remodeling and trophoblastic invasion have defects leading to characteristic hypertensive disorders of pregnancy and fetal growth restriction [18,19].

Pathophysiology of Preeclampsia

Defects in spiral artery remodeling and trophoblast invasion result in impaired placentation and placental ischemia, the primary events leading to placental release of soluble factors causing systemic endothelial dysfunction in the preeclamptic phenotype.

Hypoperfusion appears to be both a cause and a consequence of abnormal placental development.

With the progression of pregnancy, the abnormal uterine vasculature is unable to accommodate the normal rise in blood flow to the feto-placental unit, resulting in hypoperfusion as gestational age increases [20-22].

Late placental changes consistent with ischemia include:

- Atherosis (lipid-laden cells in the wall of the arteriole)
- Fibrinoid necrosis
- Thrombosis
- Sclerotic narrowing of arterioles
- Placental infarction [23-27]

Defects in placentation are associated with multiple adverse pregnancy outcomes, including [94]:

- 2nd trimester fetal death
- Placental infarcts
- Abruptio placentae
- Preeclampsia with or without intrauterine growth restriction
- Intrauterine growth restriction without maternal hypertension
- Premature rupture of membranes (PROM)
- Preterm labor (PTL) [94]

Pathophysiology of Preeclampsia

Critical components in the pathogenesis of preeclampsia include:

- Hypoperfusion
- Hypoxia
- Ischemia

The release of factors into the maternal blood stream alters the maternal endothelial cell function, leading to characteristic systemic signs and symptoms of preeclampsia [28-32].

Hypoperfusion becomes more pronounced as pregnancy progresses, since the abnormal uterine vasculature is unable to accommodate the normal rise in blood flow to the fetus/placenta with increasing gestational age [20-22].

It is unknown why the normal development of uteroplacental circulation, does not occur in some pregnancies.

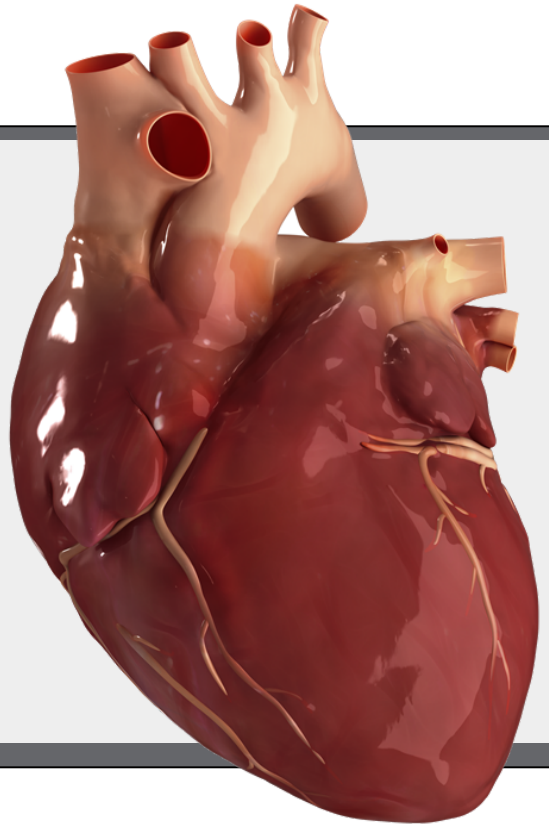
The following are suspected to play a role:

- Vascular
- Environmental
- Immunological
- Genetic factors [35]

Delivery of the placenta is the cure for preeclampsia [35].

Click for a video on preeclampsia

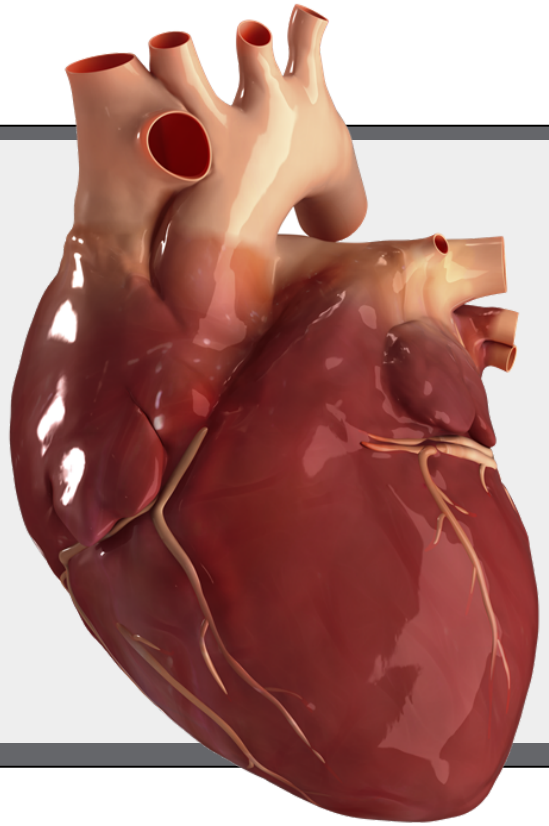
https://www.youtube.com/watch?v=70tpqg58Oug



CARDIAC PHYSIOLOGY

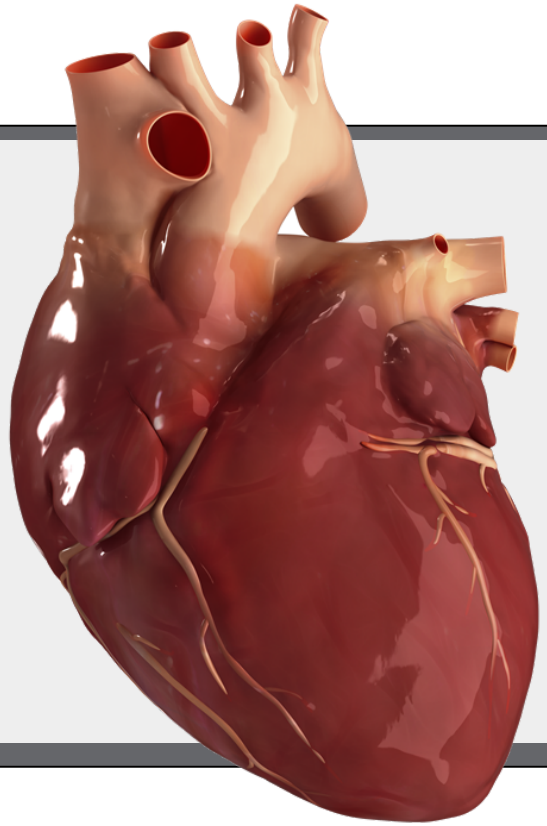
Hypertension is the earliest clinical finding of preeclampsia and is the most common clinical indicator of disease.

Hypertension can develop at any point after 20 weeks gestation or in the postpartum period.



CARDIAC PHYSIOLOGY

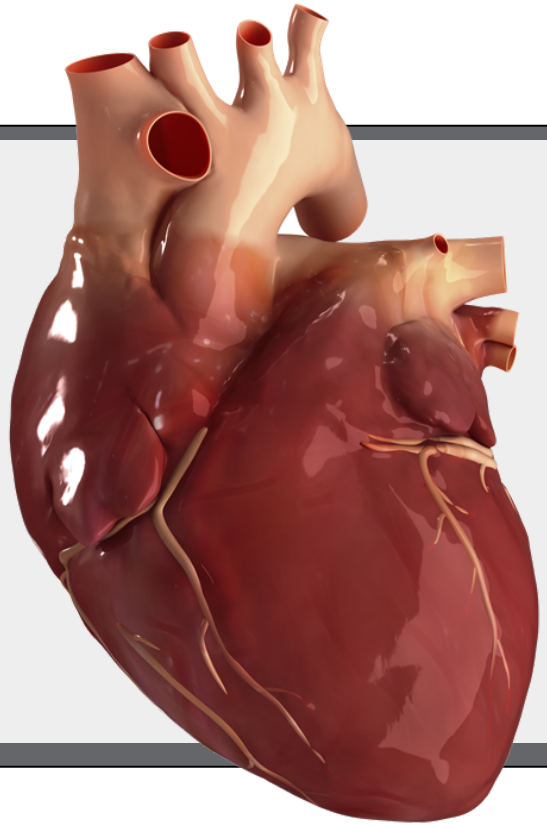
- The BP usually rises gradually to ≥140/90mmHg.
  - Often in the third trimester and after the 37th week of gestation [28].
- A woman with a systolic blood pressure greater than or equal to 140 mmHg or a diastolic blood pressure greater than or equal to 90 mmHg on 2 occasions at least 4 hours apart after 20 weeks gestation is concerning for pre-eclampsia.
- A woman with a systolic blood pressure greater than or equal to 160 mmHg or a diastolic blood pressure greater than or equal to 110 mmHg is concerning for pre-eclampsia with severe features.
- The diagnosis is confirmed if the severe range BP is noted on two occasions at least 4 hours apart; however, antihypertensive therapy should not be withheld for the purposes of confirming the diagnosis.



CARDIAC PHYSIOLOGY

Vascular Changes

- Typical vascular changes include:
  1. Vasospasm
  2. Leaky capillaries
- Vasospasm is caused by inappropriate ratios of the vasoconstrictors - thromboxane A2 and endothelins - and vasodilators - prostacyclin and nitric oxide
- Leaky capillaries are caused by innate differences of the vasculature, in addition to decreased colloid oncotic pressure
- The vascular changes are responsible for the common finding of edema, as well as the cause of the increased risk of pulmonary edema

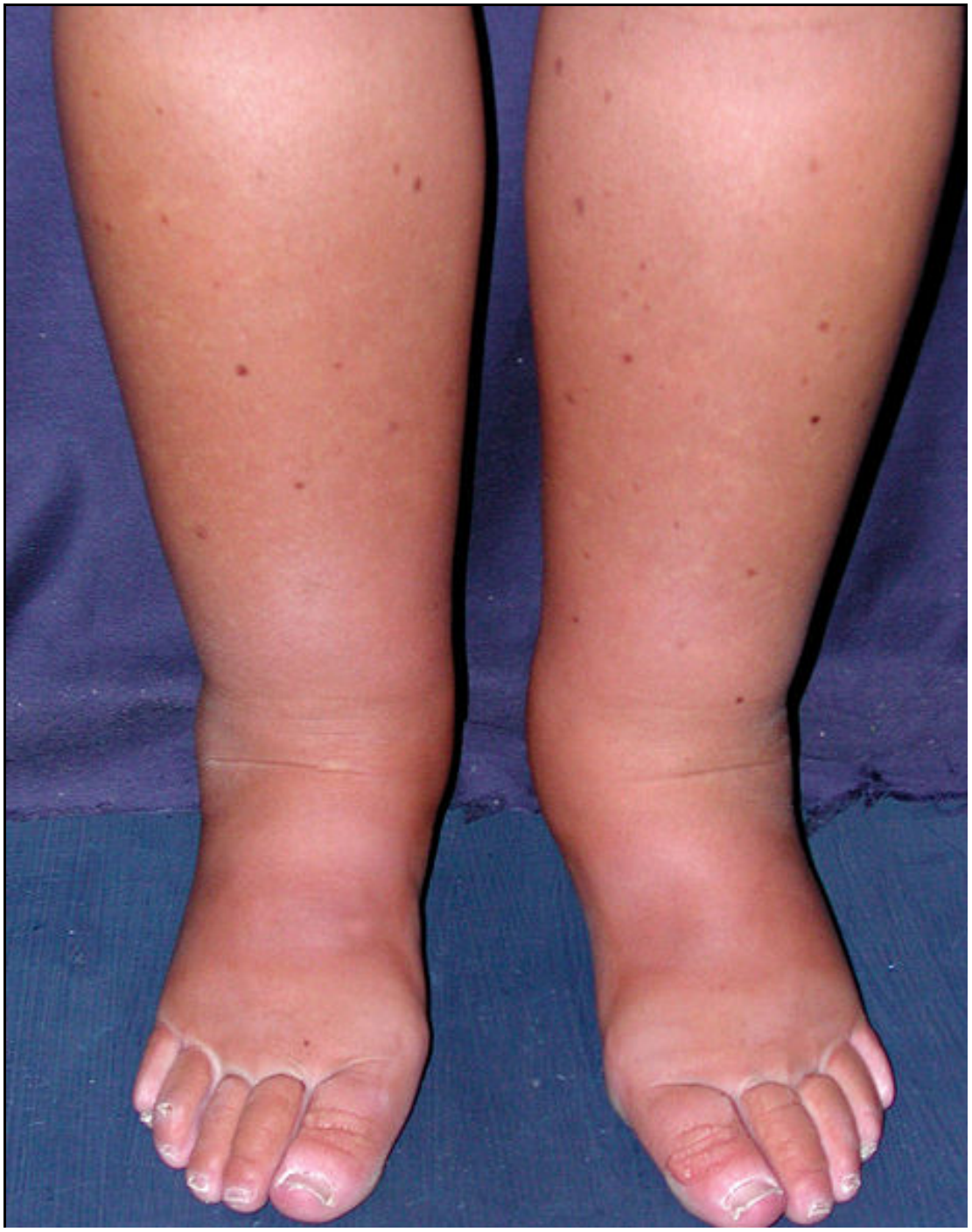


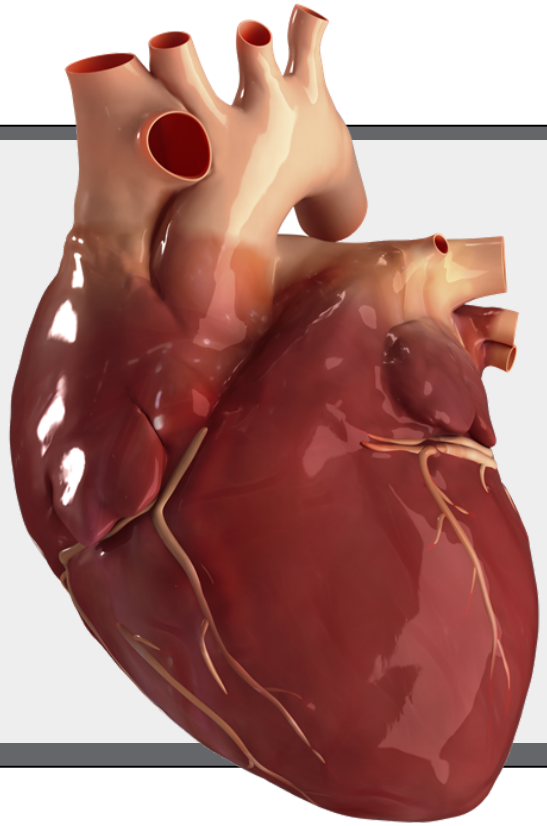
CARDIAC PHYSIOLOGY

Edema

- Edema is one of the most common findings in preeclampsia
- The finding is likely related to leaky capillaries and decreased colloid oncotic pressure.
- Edema is not part of the diagnostic criteria for preeclampsia due to the frequency of this finding in most pregnant women; however, if rapid onset edema or weight gain is noted, it can be a harbinger for the future development of preeclampsia.

Click to see a picture of edema in the lower extremities





CARDIAC PHYSIOLOGY

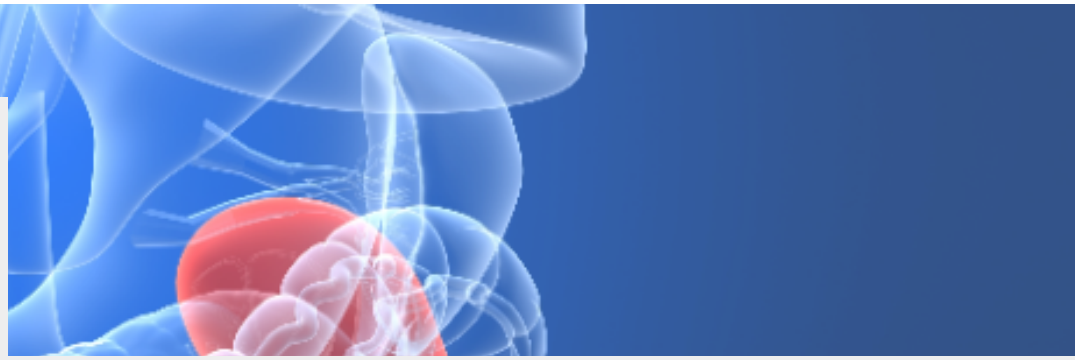
- Can be associated with a highly variable hemodynamic profile [36-41].
  - A small subgroup of women develops myocardial damage or diastolic dysfunction [41].
- Myocardial function is usually unchanged; however, in isolated cases, there can be a reduction in left ventricular function.
- BNP can be elevated, likely secondary to elevated cardiac afterload [45].
- Troponins should not be elevated in the setting of preeclampsia; if elevated troponins are noted, investigation for alternative etiologies should be sought [53].

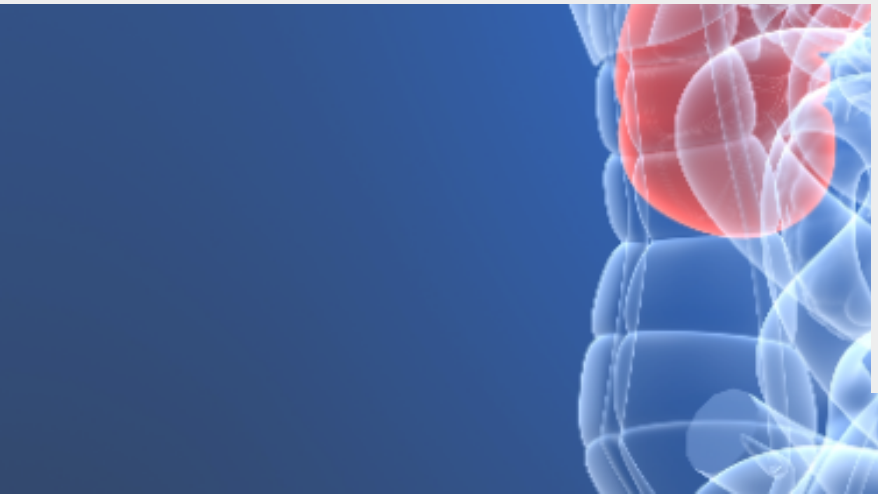
Pulmonary Physiology

- Diagnosed by chest x-ray showing typical features of pulmonary edema.
- Caused by capillary leak and decreased colloid oncotic pressure.
- If present, indicative of preeclampsia with severe features.
- More common in the postpartum period [54, 57].

Clinical Features of the Renal System

The kidney is the organ most likely to manifest endothelial injury related to preeclampsia.





Renal - Proteinuria

The most common cause of proteinuria in pregnant women is preeclampsia.

Click here to see more information.

Typical renal changes include:

1. Proteinuria
2. Elevated creatinine

- The histopathologic renal finding is glomerular endotheliosis.
- Proteinuria is caused increased tubular permeability.
- Increased creatinine is caused by acute renal deterioration, which is likely related to vasospasm causing a decrease in the glomerular filtration rate.

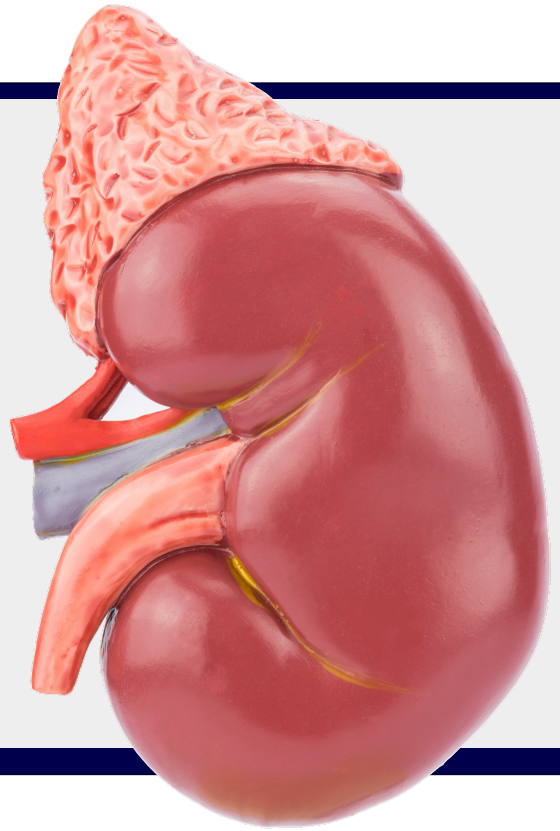
Click here to see more information.

Proteinuria is defined as:

- >0.3 mg protein on urine protein:creatinine ratio
- >300 mg of protein in a 24-hour specimen.
- Persistent 1+ (30mg/dL) on dipstick.

Proteinuria

- Once diagnostic proteinuria is noted, there is typically no reason to continue to trend values.
- Proteinuria is caused by impaired integrity of the glomerular filtration barrier.
- Protein excretion increases with hypofiltration caused by altered tubular function [42].



RENAL FUNCTION

Glomerular filtration rate (GFR) decreases by 30 to 40% in preeclampsia.

Plasma creatinine is typically normal or slightly elevated (0.8-1.2 mg/dL).

Creatinine > 1.1mg/dL or doubling of a baseline value indicates severe disease.

- Caused by renal vasoconstriction and sodium retention due to reduced plasma volume and systemic vasoconstriction.

Urine output may decrease to <500mL/24 hours.

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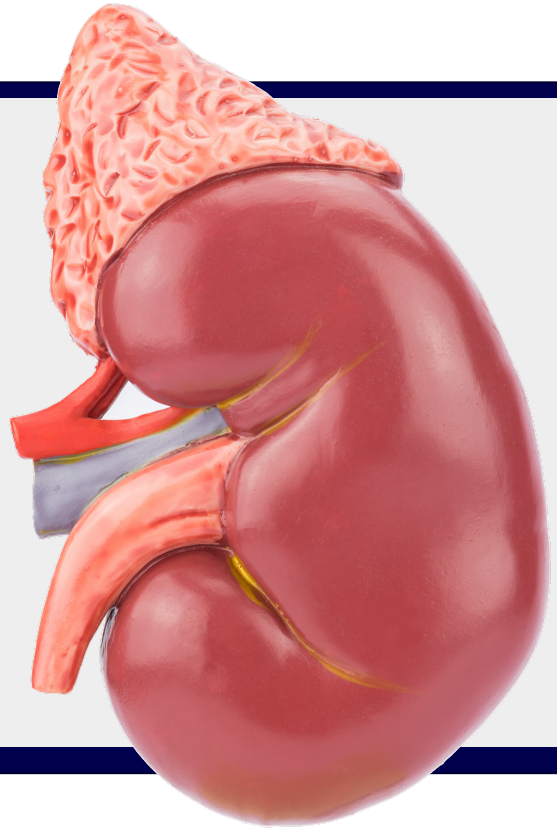

RENAL FUNCTION

The role of serum uric acid levels remains controversial as a predictor of complications associated with preeclampsia [43,44].

An international prospective study of women with preeclampsia demonstrated that serum uric acid, based upon gestational age:

- Is not clinically useful in predicting adverse maternal outcomes.
- Is useful in predicting perinatal outcomes [45].

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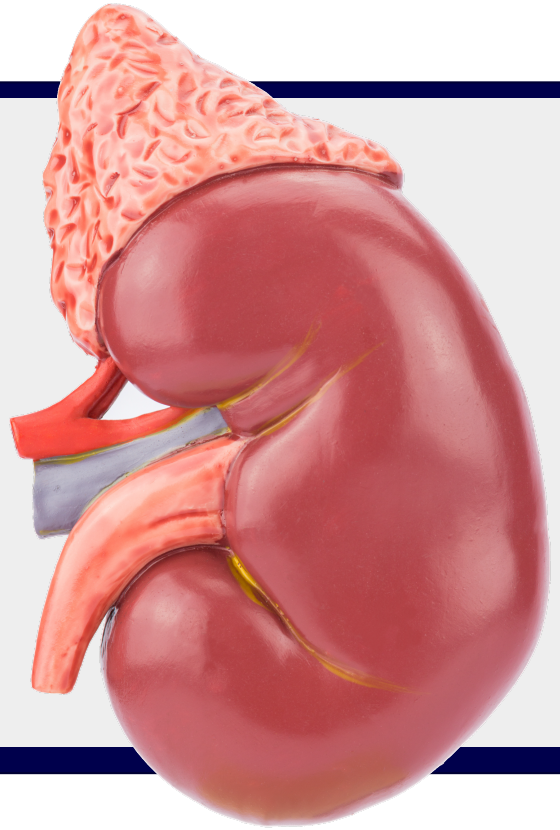


RENAL FUNCTION

Histology findings include:

- Endothelial cell swelling
- Loss of fenestrations
- Occlusion of capillary lumens [46]

Glomerular Endotheliosis

- Shares histologic features with non-preeclamptic thrombotic microangiopathies [46].
- Histopathologic finding due to preeclampsia

Click through all 3 slides before moving on to the next page.

Hematologic Changes

- Typical hematologic changes include:
  1. Hemoconcentration
  2. Thrombocytopenin
  3. Possible hemolysis
- Hemoconcentration is caused by a lack of hypervolemia, which is attributed to the leaky capillaries.
- Thrombocytopenia is caused by increased platelet activation, aggregation and consumption.
- The hemoglobin level should take into account the possibility of hemoconcentration and hemolysis.
- Lactate dehydrogenase is highly concentrated in red blood cells; therefore, an elevated LDH (>600) is indicative of hemolysis.

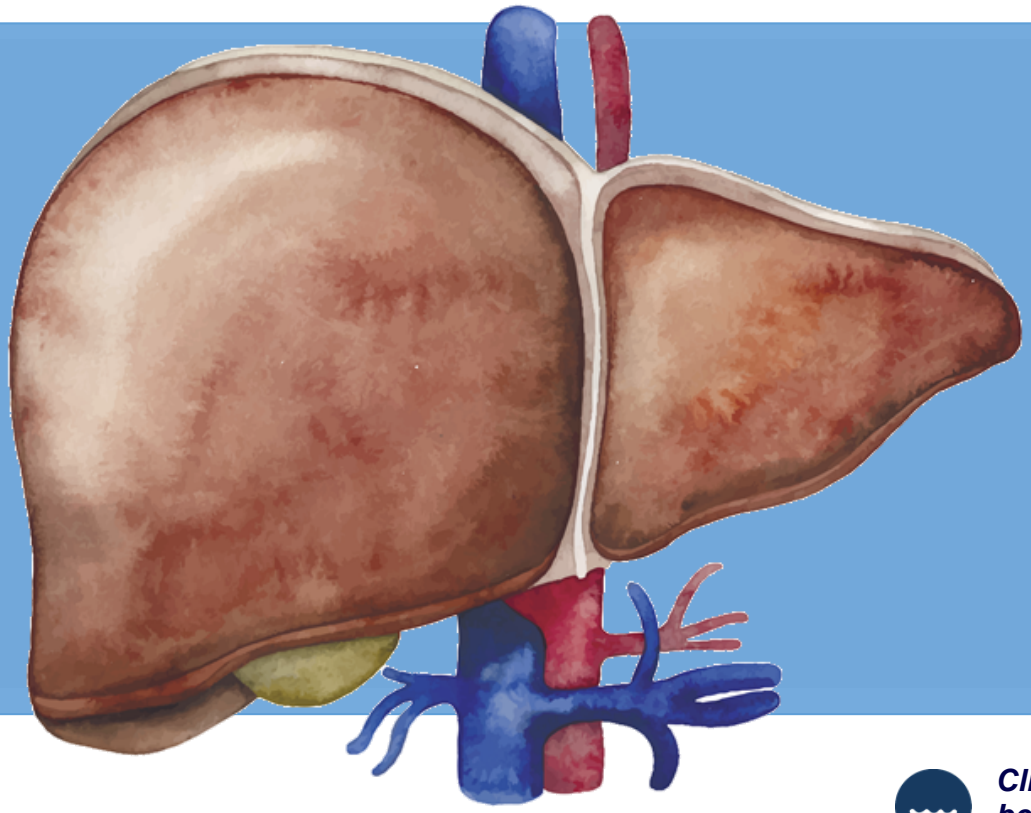
When hemolysis and reduced plasma volume are both present, the hematocrit may be normal.

White blood cell (WBC) count may be slightly elevated due to neutrophilia.

Concentrations of the following are not affected unless abruptio placenta or severe liver dysfunction is also present:

- Prothrombin time (PT)
- Partial thromboplastin time (PTT)
- Fibrinogen [47]

HEPATIC



Histologic findings observed in the livers of preeclamptic women [48,49]:

- Periportal fibrin deposits
- Sinusoidal fibrin deposits
- Microvesicular fat deposits

Reduced hepatic blood flow can lead to:

- Ischemia
- Periportal hemorrhage

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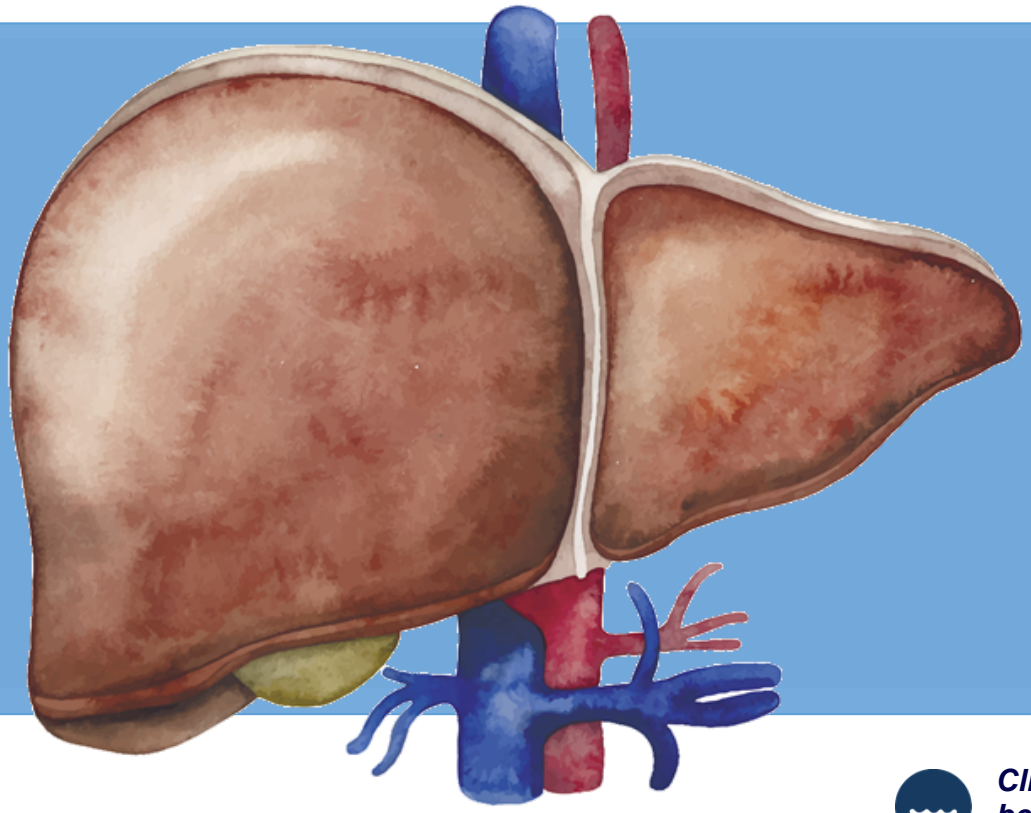
HEPATIC



Hepatic Changes

- Typical hepatic changes include:
  1. Elevated AST, ALT
  2. Elevated LDH
- AST is the dominant transaminase that is released into peripheral circulation secondary to periportal necrosis.
- Typically, early in the course of the disease, AST is elevated more significantly than ALT.
- LDH can be elevated from hemolysis, but also from hepatic dysfunction if there is liver ischemia or necrosis.
- In rare cases, elevated bilirubin can be seen if there is significant hemolysis in the late stage of disease.
- If hepatic function is severely compromised, there can be abnormalities in coagulation studies including PT, PTT and fibrinogen.

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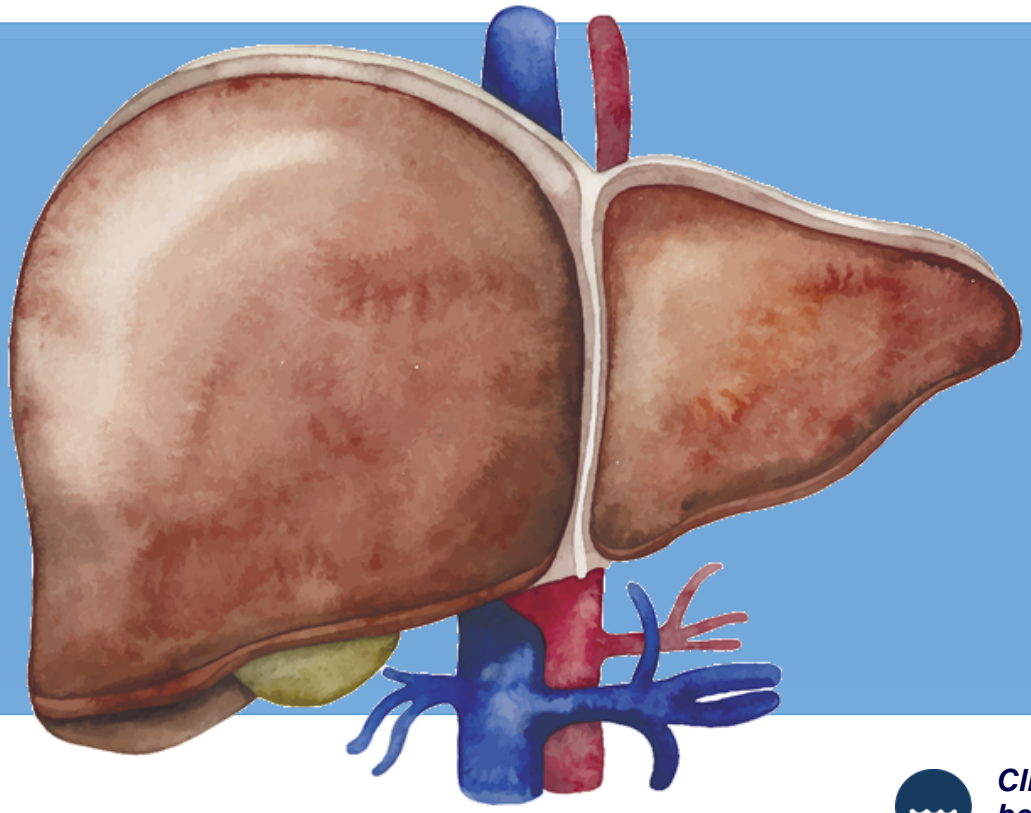
HEPATIC



Hepatic Function

- Impaired liver function that is not accounted for by alternative etiology and is consistent with transaminases that are 2x the upper limit of normal is consistent with preeclampsia with severe features.
- The diagnosis can also be made with severe, persistent right upper quadrant pain or epigastric pain unresponsive to medications in the setting of hypertension.

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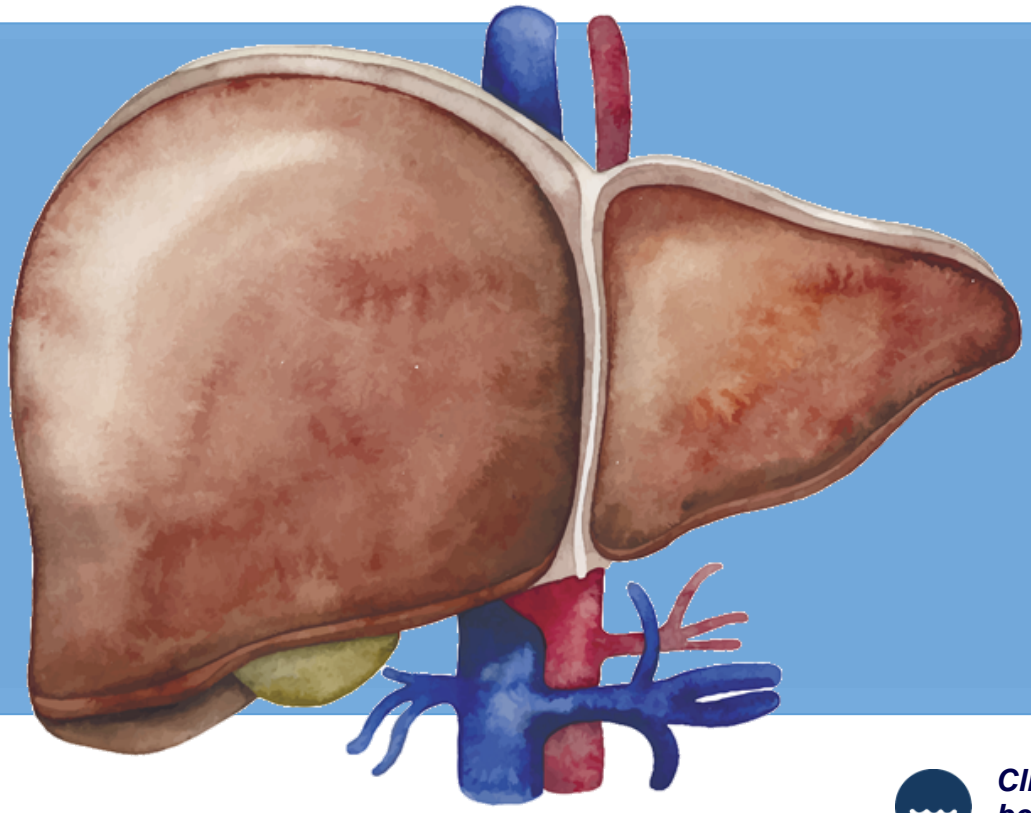
HEPATIC



Epigastric Pain

Thought to be related to stretching of the Glisson's capsule due to hepatic swelling or bleeding.

May be the only presenting symptom of preeclampsia

- Can be mistaken for gastroesophageal reflux.
- Liver irritation can also present as new onset nausea or vomiting
- GERD is common for pregnant women and occurs more often at night.

Palpation of the liver may cause her discomfort.

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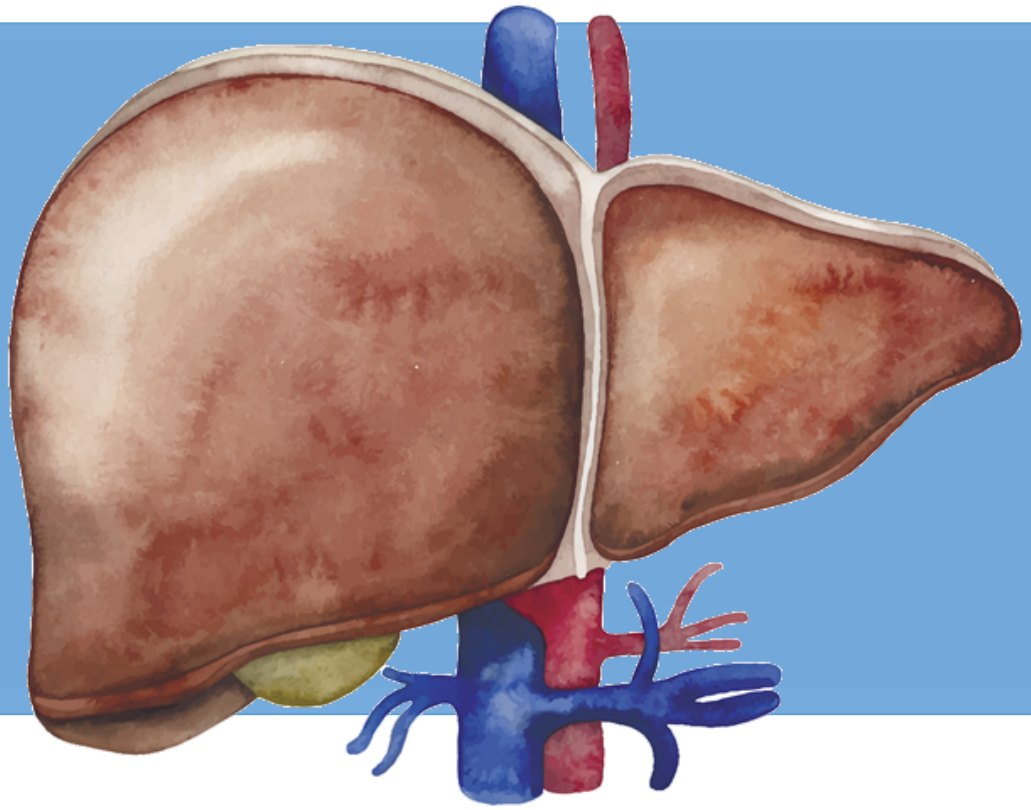
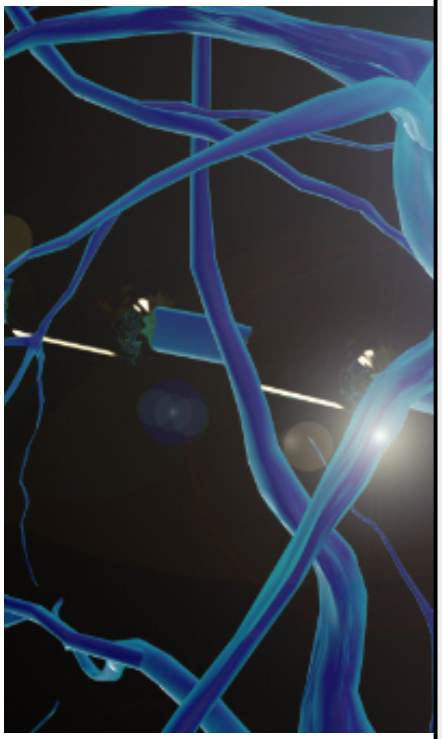
HEPATIC



Transient diabetes insipidus has been reported in preeclampsia with hepatic dysfunction; but is a rare occurrence.

Further discussion of diabetes insipidus is beyond the scope of this program.

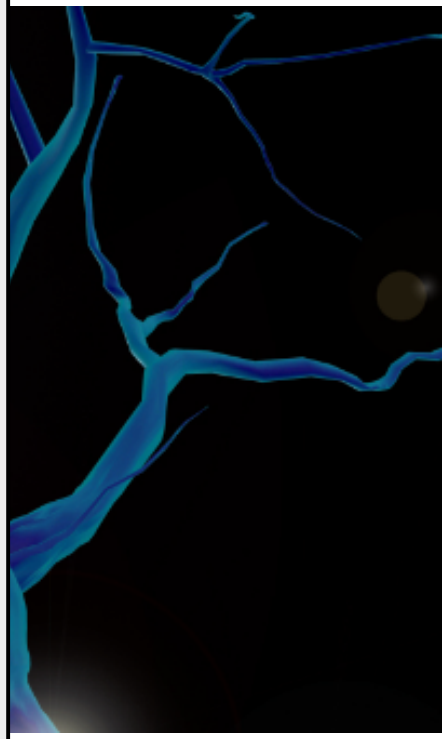
Diabetes insipidus would present with unquenchable thirst in the setting of profuse polyuria.

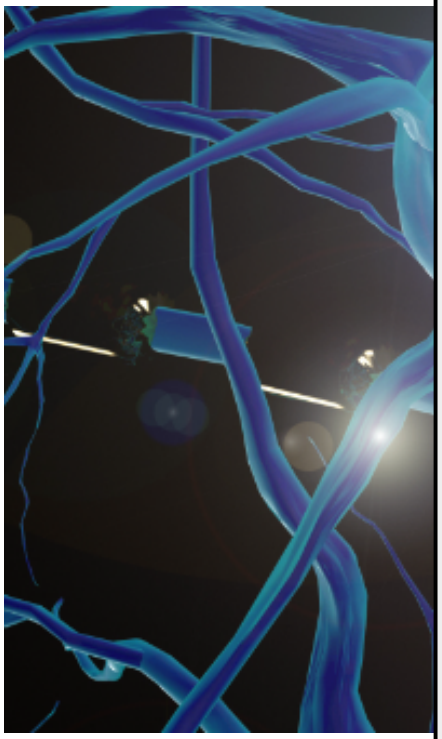


Central Nervous System (CNS)

Central nervous system manifestations of preeclampsia include:

- Headache
- Visual symptoms
- Generalized hyperreflexia
- Sustained ankle clonus





CNS

Headache may be:

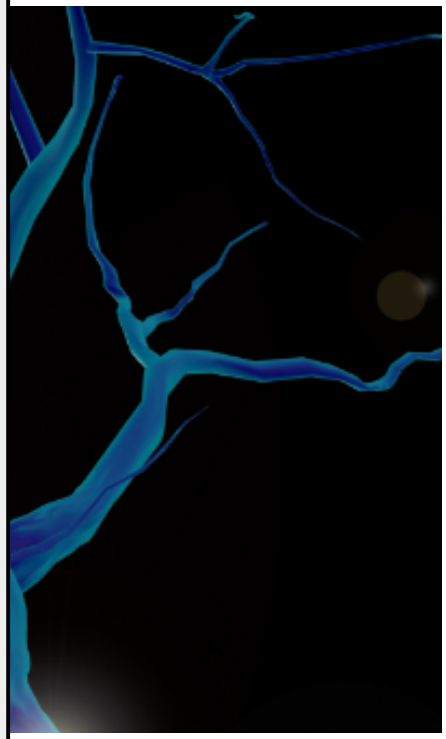
- Temporal
- Frontal, the most common site
- Occipital
- Diffuse [50,51]

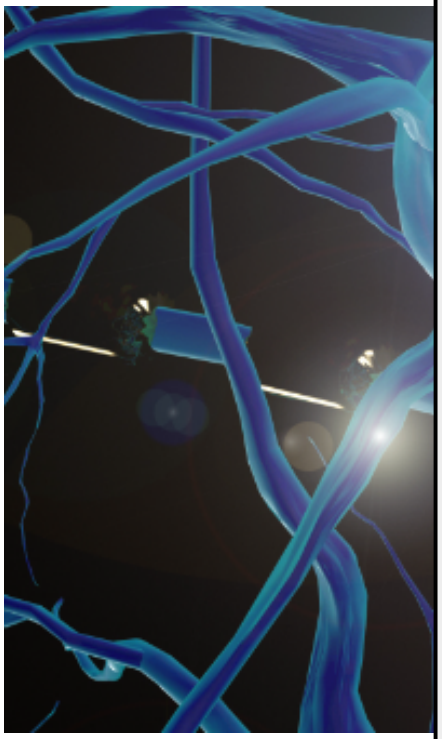
Frontal is most common.

Pain described as:

- Throbbing
- Pounding
- Piercing

The headache is not relieved with over-the-counter analgesics and persists despite sleep, caffeine and eating.



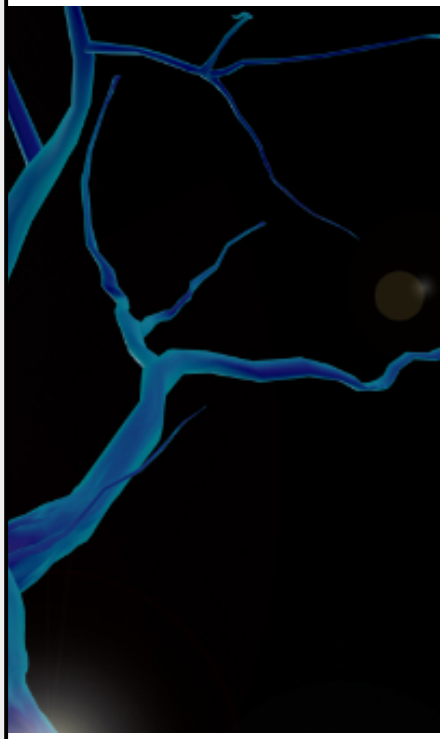


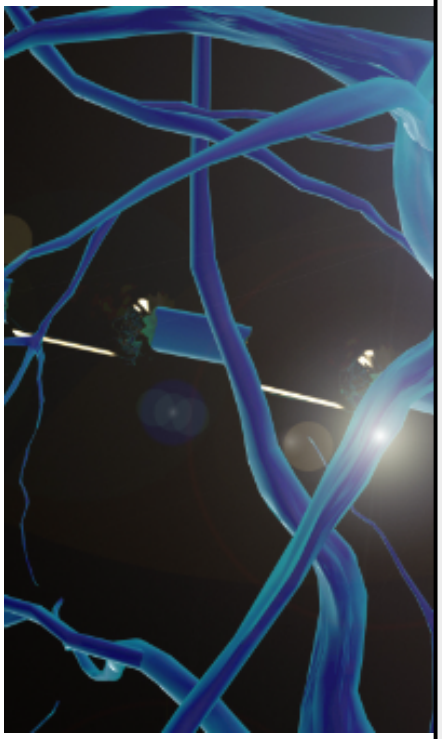
CNS

Visual symptoms are caused by retinal arteriolar spasm [52].

Symptoms include:

- Blurred vision
- Flashing lights or sparks (photopsia)
- Scotomata (dark area or gaps in the visual field [53-55]
- Diplopia (blindness in one eye)
- Cortical blindness is rare and typically transient [56]





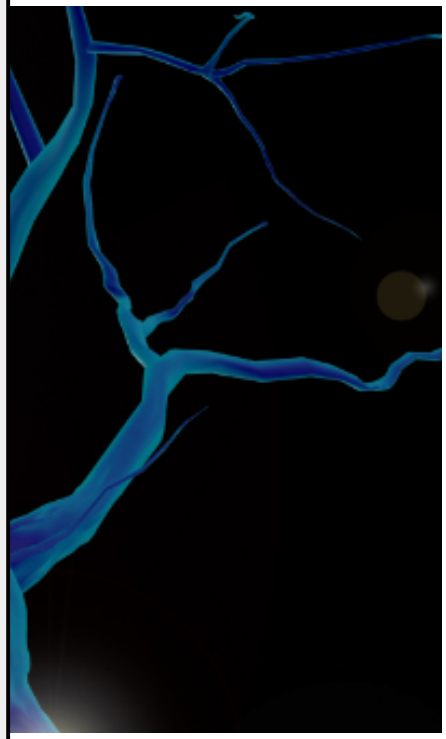
CNS Seizures

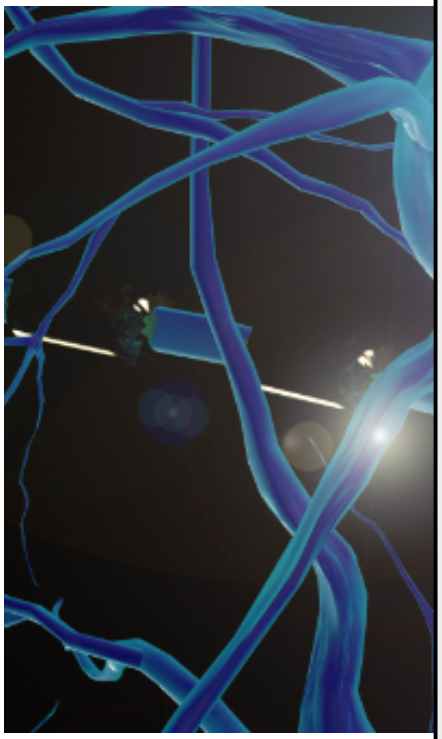
When a seizure occurs in a woman with preeclampsia, it signifies eclampsia.

- 1 in 400 women with preeclampsia without severe features develop eclamptic seizures [3].
- 1 in 50 with preeclampsia with severe features women will develop eclamptic seizures [5-11].

Risks associated with an eclamptic seizure include:

- Hemorrhage
- Petechiae
- Cerebral edema
- Vasculopathy
- Ischemic brain damage
- Microinfarcts [87]

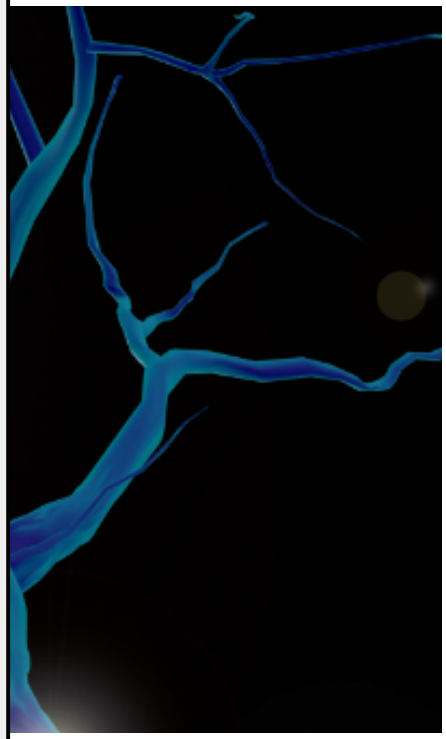


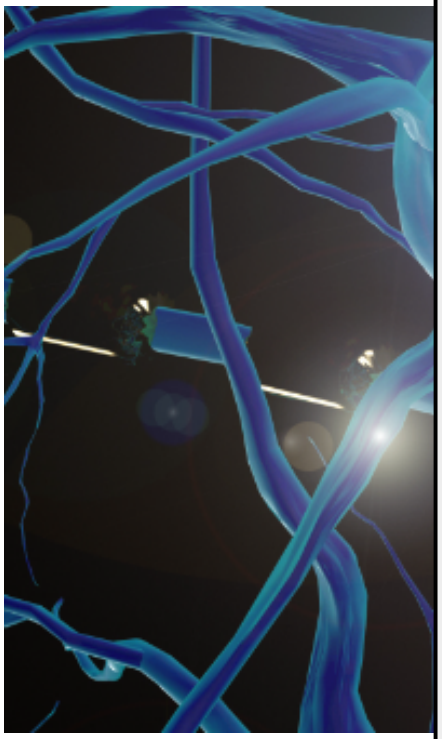


CNS

Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) findings may include:

- Cerebral edema
- Cerbral ischemia
- Hemorrhagic changes [58,59]
- Posterior reversible leukoencephalopathy syndrome (PRES):
  - Brain abnormalities associated with preeclampsia are caused by generalized endothelial cell dysfunction and loss of cerebrovascular autoregulation [92].



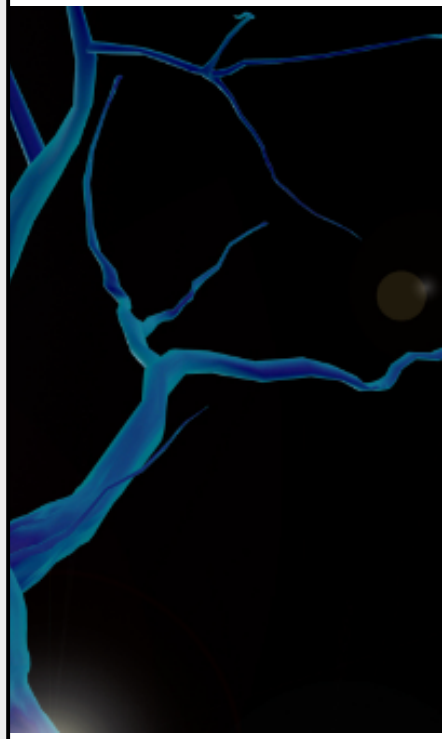


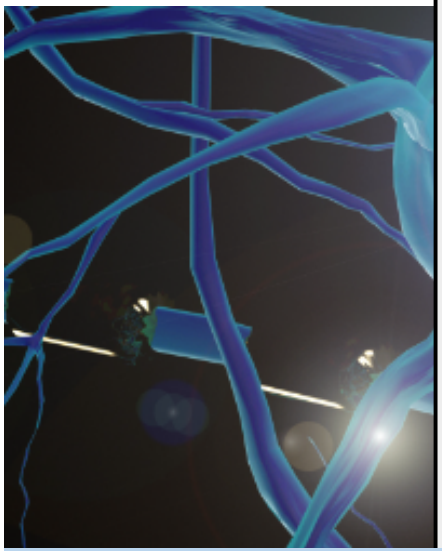
CNS – Stroke

Leading cause of death or disability related to severe preeclampsia or eclampsia [93].

Most strokes caused by preeclampsia or eclampsia are:

- Hemorrhagic
- Preceded by severe headache
- Sustained severe range blood pressure



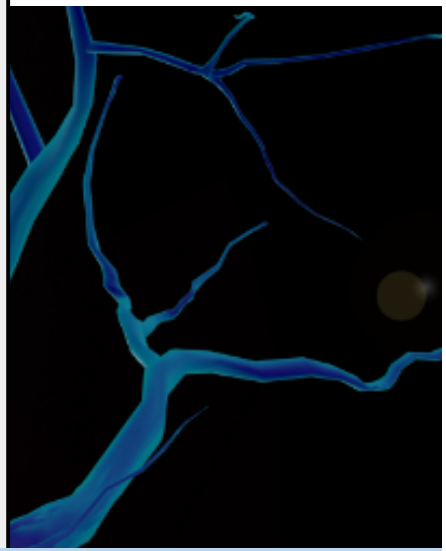


CNS – Stroke

Eclamptic seizures do not occur in all cases.

Risk factors for hemorrhagic stroke in women with preeclampsia include:

- Systolic BP persistently > 160mmHg and/or
- Diastolic BP persistently > 110mmHg
- Severe headache
- Seizures



Prompt treatment of severe range blood pressures in the setting of preeclampsia is indicated in order to prevent stroke

Pathophysiology of Preeclampsia

Fetus

Fetal Growth Restriction:

- Severe and early onset of preeclampsia affects birth weight [60].
- Although fetal growth restriction is not part of the diagnosis of preeclampsia, the finding of fetal growth restriction is a risk factor for the subsequent development of preeclampsia

Oligohydramnios

- Can develop in the setting of preeclampsia due to placental insufficiency

Early Onset Severe Preeclampsia Increases the Risk of:

- Fetal death
- Perinatal death
- Severe neonatal morbidity [61,62]

Abruptio Placenta

Occurs in < 1% of women with preeclampsia without severe features.

Occurs in 3% of women who have severe features [64].

If placental abruption occurs in the setting of pre-eclampsia, the patient has a high risk of fetal demise, in addition to a high risk for coagulopathy, including disseminated coagulopathy.

This **summary table** reviews features of preeclampsia with adverse and severe features.

System	Severe Feature
Central Nervous System (CNS)	• Headache • Visual Changes
Cardiac	• SBP>160 or DBP>110
Hematologic	• Platelets <100,000
Hepatic	• AST, ALT > 2x upper limit of normal
Renal	• Creatinine >1.1 or 2x baseline

If pre-eclampsia with severe features develops prior to 37 weeks, preterm delivery is indicated.

- This may be indicated within hours to days of diagnosis

Preeclampsia does not accelerate fetal maturation.

In preeclamptic women with age-matched normotensive controls, frequency of the following neonatal morbidities is not increased:

- Neonatal respiratory distress
- Intraventricular hemorrhage
- Necrotizing enterocolitis (NEC) [63]

A critical factor in reducing maternal mortality is early recognition and treatment of worsening signs and symptoms of preeclampsia. Health care providers often fail to recognize and respond to clinical signs and symptoms in a timely manner.

In fact, missed vital sign 'triggers' occurred in 60% of preeclampsia deaths [99].

This module will help with the development of this critical thinking, but each center must develop a process for recognition and response to patient's deteriorating conditions with written criteria describing early warning signs and indicating when to seek further assistance [100].

It is imperative to the health of the mother and fetus to communicate worsening signs and symptoms of worsening or severe preeclampsia to the provider if they are present:

- Headache
- Increasing BP
- Altered consciousness: restless, agitation, hallucinations, lethargy, confusion
- Visual disturbances: floaters, blurred vision, spots, blind spots
- Upper abdominal pain
- Urine output < 30mL/hour
- Shortness of breath
- Complaints of chest pain
- Pulse oximetry < 95%
- Cough
- Tachypnea > 26 breaths/min
- Tachycardia > 100 bpm
- Adventitious breath sounds
- Eclamptic seizure
- Magnesium toxicity [101]

This link provides a tool for preeclamspia early recognition (PERT) to help: https://www.health.ny.gov/publications/2036.pdf

New York State Department of Health **Preeclampsia Early Recognition Tool (PERT)**

ASSESS	NORMAL (GREEN)	WORRISOME (YELLOW)	SEVERE (RED)
Awareness	Alert/oriented	• Agitated/confused • Drowsy • Difficulty speaking	• Unresponsive
Headache	None	• Mild headache • Nausea, vomiting	• Unrelieved headache
Vision	None	• Blurred or impaired	• Temporary blindness or blind spots
Systolic BP (mm Hg)	100-139	140-159	≥160
Diastolic BP (mm Hg)	50-89	90-109	≥110
HR	61-110	111-129	≥130
Respiration	11-24	25-30	<10 or >30
SOB	Absent	Present	Present
O2 Sat (%)	≥95	91-94	≤90
Pain: Abdomen or Chest	None	• Nausea, vomiting • Chest pain • Abdominal pain	• Nausea, vomiting • Chest pain • Abdominal pain
Fetal Signs	• Category I • Reactive NST	• Category II • IUGR • Non-reactive NST	• Category III
Urine Output (ml/hr)	≥50	30-49	≤30 (in 2 hrs)
Proteinuria (Level of proteinuria is not an accurate predictor of pregnancy outcome)	Trace	• ≥ 1+** • ≥300mg/24 hours	• 3+ or greater on 2 samples 4 hours apart*** • ≥ 5 Gms/24 hours***
Platelets	>100	50-100	<50
AST/ALT	normal	1-<2x normal	2x normal or greater
Creatinine	≤0.8	0.9-1.1	≥1.2
Magnesium Sulfate Toxicity	• DTR +1 • Respiration 16-20	• Depression of patellar reflexes	• Respiration <12

GREEN = NORMAL

Proceed with Protocol

YELLOW = WORRISOME

Increase assessment frequency

# Triggers	TO DO
1	• Notify provider & charge nurse
≥2	• Notify provider & charge nurse • In-person evaluation • Order labs/tests • Anesthesia consult • Consider magnesium sulfate • Supplemental oxygen

** Physician should be made aware of worsening or new-onset proteinuria.

RED = SEVERE

Trigger: 1 of any type listed below	TO DO
1 of any type	• Notify provider & charge nurse • Immediate evaluation • Transfer to higher acuity level • 1:1 staff ratio
Awareness	• Consider Neurology consult
Headache	• CT Scan
Visual	• R/O SAH/Intracranial hemorrhage
BP	• Labetalol/hydralazine in 15 minutes • Magesium sulfate loading or maintenance infusion
Chest pain	• EKG, Consider CT angiogram
Respiration	• O2 at 10L per rebreather mask
SOB	• R/O pulmonary edema
O2 SAT	• Chest x-ray

*** Results signify massive proteinuria and physician should be notified. Although massive proteinuria has been eliminated from the consideration of preeclampsia as "severe", physician should be made aware of worsening or new-onset proteinuria.

New York State nyspQc Perinatal Quality Collaborative

NEW YORK STATE Department of Health

Citation: Maurice L. Druzin, MD, Laurence E. Shields, MD, Nancy L. Peterson, RNC, PNNP, MSN, Kathryn Melsop, MS, Valerie Cape, BS, BA. Preeclampsia Toolkit: Improving Health Care Response to Preeclampsia (California Maternal Quality Care Collaborative Toolkit to Transform Maternity Care) Developed under contract #11-10006 with the California Department of Public Health; Maternal Child, and Adolescent Health Division; Published by the California Maternal Quality Care Collaborative, August 2013.

The funding for the development of the toolkit was provided by Federal Title V block grant funding from the California Department of Public Health: Maternal, Child and Adolescent Health Division and Stanford University.

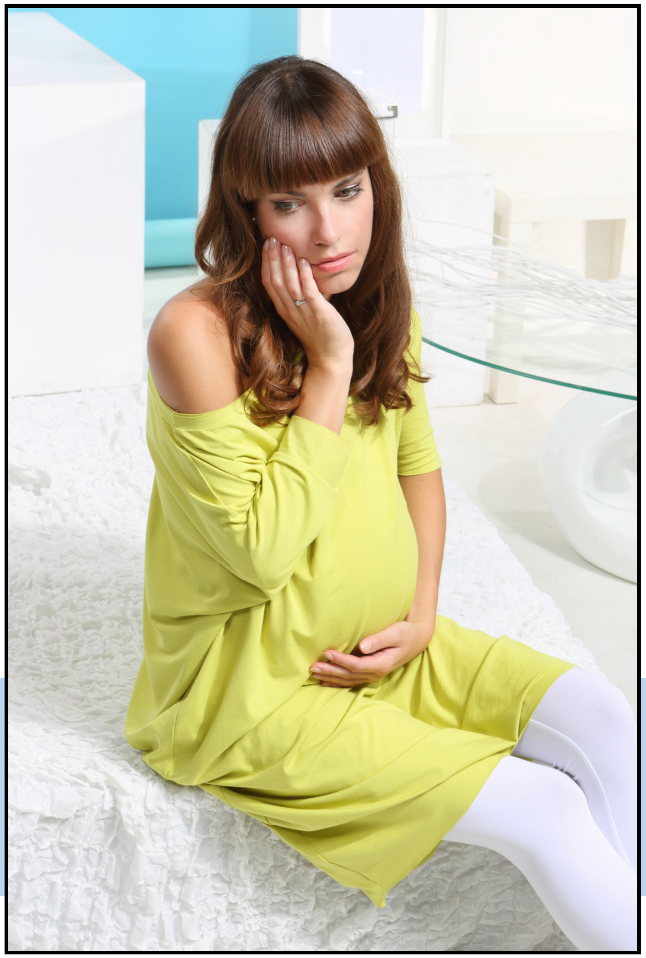
Risk Factors for Preeclampsia

Nulliparity

Exposure to paternal antigens is associated with the pathogenesis of preeclampsia. The primigravid woman, in theory, may be at risk due to limited exposure [65].

Risk Factors for Preeclampsia are Related to:

- Ethnicity: Nordic, Black, South Asian, and Pacific Island
- Low socioeconomic class
- Advanced maternal age
- Obesity
- Assisted reproductive technology
- Obstructive sleep apnea



Risk Factors for Preeclampsia

- Preeclampsia in a previous pregnancy
  - The severity of preeclampsia strongly impacts this risk.
- If a woman developed preeclampsia with severe features in the second trimester of a prior pregnancy, the risk of recurrence is 25-65% [66-69].
- If a woman has a history of pre-eclampsia without severe features, the risk of recurrence is 5-7% [70,71].
- Women who had a normotensive first pregnancy develop preeclampsia in less than 1% of second pregnancies [65].

Risk Factors for Preeclampsia

- Most cases of preeclampsia occur without any family history.
- However, preeclampsia may have a hereditary aspect when a first degree relative has had preeclampsia [65].

Click each image to learn more.

Risk Factors for Preeclampsia

A mother or sister having had preeclampsia increases the risk in a woman's first pregnancy for developing preeclampsa by **2- to 5-fold** compared to a woman with no family history [72-75].

Click each image to learn more.

Risk Factors for Preeclampsia

The development of preeclampsia is more likely when a woman becomes pregnant by a man who has fathered a preeclamptic pregnancy with another woman [76].

The risk of preeclampsia is increased in a first pregnancy or short duration of exposure to her partner.

Click each image to learn more.

Risk Factors Cont'd

Risk Factors for Preeclampsia

Preexisting Medical Conditions

- Pregestational diabetes
- Chronic hypertension
- Renal disease
- Antiphospholipid antibody syndrome
- Systemic lupus erythematosus

Risk Factors for Preeclampsia

Antiphospholipid antibody syndrome (APS):

- 11-17% of women with pre-eclampsia will test positive for APS antibodies.
- The risk is highest in women who develop preeclampsia prior to 34 weeks.

Risk Factors for Preeclampsia

- Preeclampsia occurs at higher rates with multi-order gestations [77]:
  - Twins
  - Triplets
  - Quadruplets
  - The risk increases with each additional fetus

Risk Factors for Preeclampsia

- Hydrops fetalis
- Unexplained fetal growth restriction
- Personal maternal history of being was small for gestational age
- Fetal growth restriction, abruptio placenta, or fetal demise in a previous pregnancy
- Pregnancy interval of < 2 years or > 10 yrs

Risk Factors Cont'd

- Non-smoker [10]
  - Evidence has shown smoking **decreases** the risk of preeclampsia
- Gestational trophoblastic disease
- History of hydatidiform mole
- Infection:
  - Urinary tract infection (UTI)
  - Periodontal disease

Women with increased risk for preeclampsia should be placed on low dose aspirin starting at 12 weeks gestation in order to prevent preeclampsia

Diagnosis of Preeclampsia

- Any pregnant patient who is noted to have an elevated blood pressure after 20 weeks gestation should be screened for possible preeclampsia.
- History
  - Ask about headaches, visual changes, right upper quadrant pain, epigastric pain, nausea and vomiting.
- Physical Exam
  - Evaluate for altered mental status, pulmonary edema, abdominal tenderness, edema, reflexes and clonus.

Laboratory evaluation

- CBC
- CMP
- Urine protein:creatinine ratio

Consider

- Non-stress test or biophysical profile
- Obstetric growth US

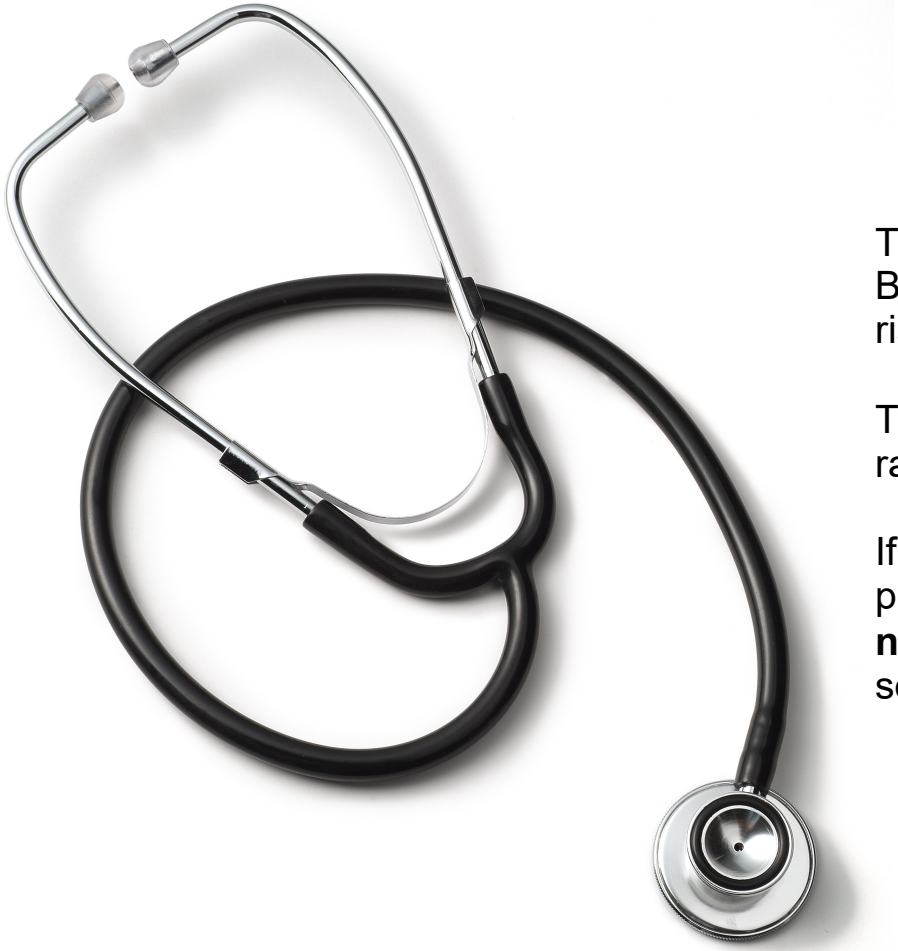
Additional Testing to Consider:

- Blood smear
- Serum lactate dehydrogenase (LDH)
- Bilirubin concentrations:
  - Microangiopathic hemolysis is suggested by elevated LDH and indirect bilirubin levels and red cell fragmentation (schistocytes or helmet cells) on peripheral blood smear.
  - Hemoconcentration occurs in preeclampsia, but hemolysis, if present, can decrease the hematocrit to normal or anemic levels.
- Coagulation function tests:
  - Prothrombin time
  - Activated partial thromboplastin time
  - Fibrinogen concentration
- Usually coagulation function tests are normal in patients without thrombocytopenia or liver dysfunction; therefore, they are not checked routinely [78].

Management of Preeclampsia

Goals in health care delivery are to prevent:

- Organ damage
- Seizures
- Cerebral vascular accidents (CVA)
- Maternal and/or fetal death



Management of Preeclampsia

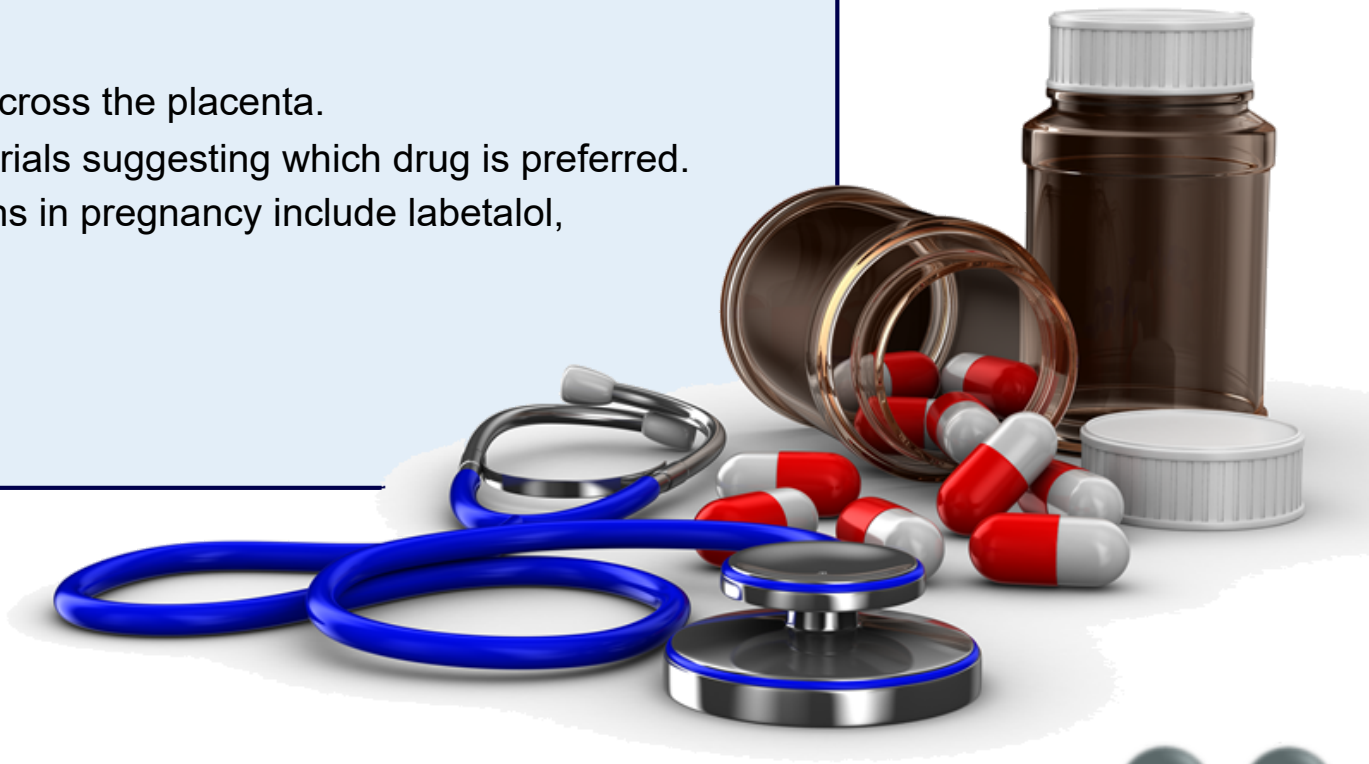
Treatment of severe hypertension is necessary when the systolic BP ≥160 mmHg and/or diastolic BP ≥110 mmHg, to reduce the risk of maternal stroke.

The goal is lower the BP, not to normal, but to a less severe range between 140-160/90-100mmHg.

If a patient meets criteria for gestational hypertension or preeclampsia without severe features, antihypertensive therapy is **not recommended** given that it can mask the diagnosis of severe blood pressures

Antihypertensive Therapy

- All antihypertensive drugs cross the placenta.
- There are no randomized trials suggesting which drug is preferred.
- Typical first-line medications in pregnancy include labetalol, hydralazine or nifedipine.



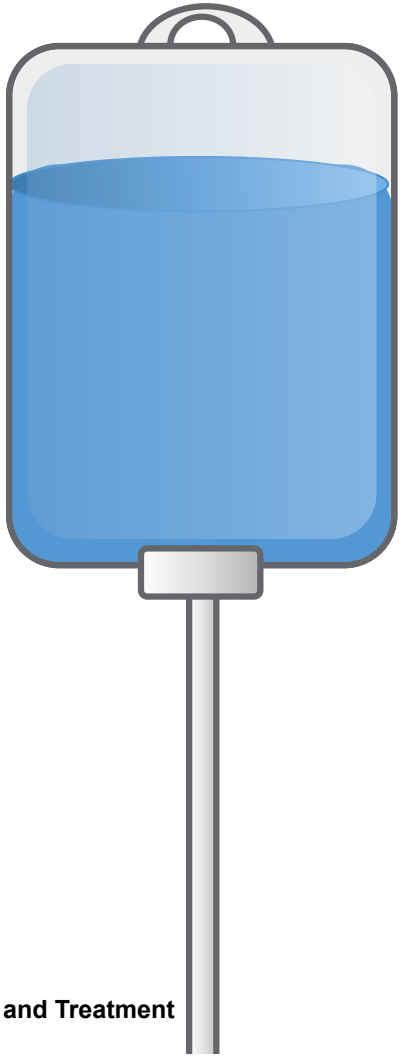
Treatment Options

- The choice of drug depends on the severity of hypertension and the route of administration:
  - Parenteral
  - Oral

Acute Therapy
First-line agents for treatment of severe hypertension:

- Labetalol
- Hydralazine
- Nifedipine, immediate release, is acceptable to above [79].

Treatment with first line agents should be expeditious and occur as soon as possible within 30-60 min of confirmed severe hypertension to reduce the risk of maternal stroke [98].



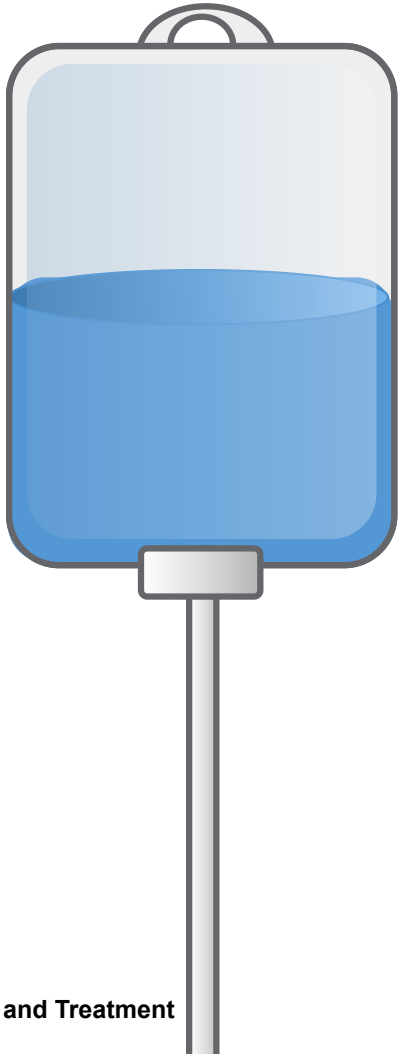
Labetalol

- First-line therapy because it is:
  - Effective
  - Rapid onset of action
  - Good safety profile

Begin with 20mg intravenously (IV) over 2 minutes followed at 10-minute intervals with incrementally larger doses up to 80 mg, up to a maximum total cumulative dose of 300 mg.

Labetalol should not be used in women with asthma, heart disease, or congestive heart failure (CHF) [98].

Click the I.V. bag to see types of treatment.



Hydralazine

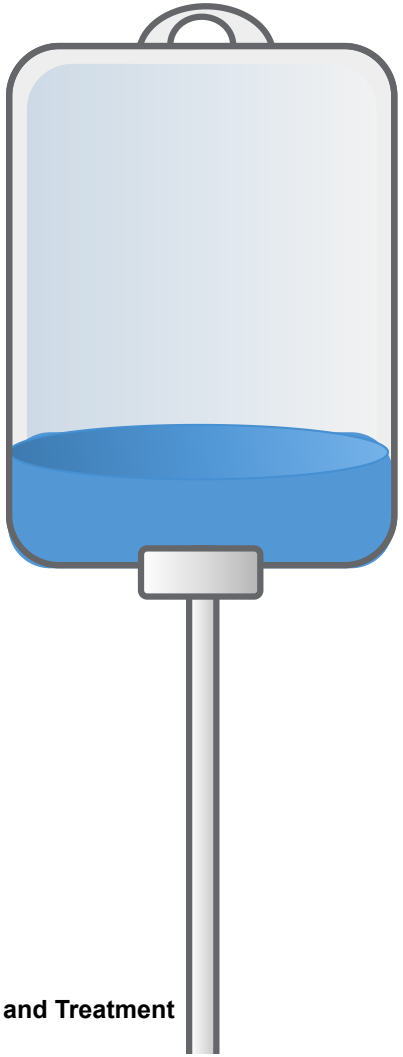
Begin with 5mg IV over 1 to 2 minutes:

- If BP goal is not achieved within 20 minutes, give a repeat dose of 5 or 10 mg. The maximum cumulative dose is 20 mg.

If a total dose of 30mg does not achieve optimal BP control, another agent should be used.

The fall in BP begins within 10 to 30 minutes and lasts for 2 to 4 hours.

Click the I.V. bag to see types of treatment.



Nifedipine - Calcium Channel Blocker (CCB)

Immediate release oral nifedipine capsules should be administered orally [98].

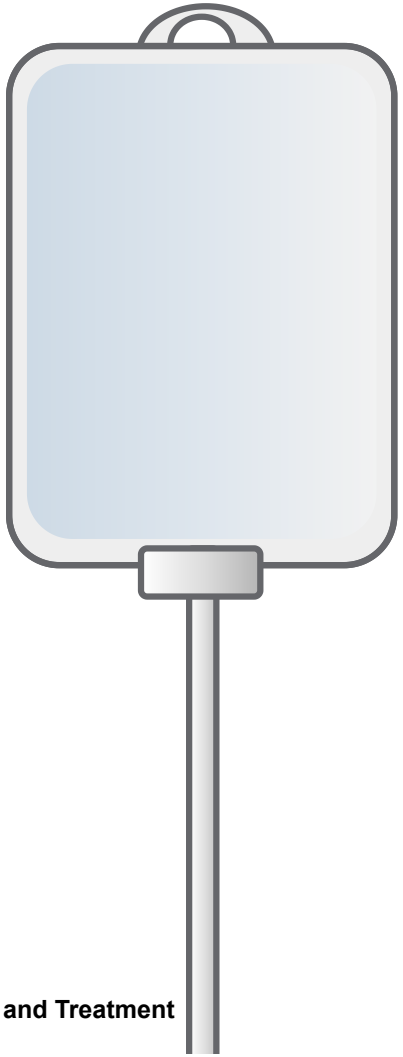
Typical dosing is 10-20 mg orally, repeated in 20 minutes, if needed, then 10-20 mg every 2-6 hours.

- Maximum daily dose is 180 mg.

Sustained release nifedipine is not recommended for acute treatment of severe range blood pressures, but can be effective in long term management.

Target BP reached within 23 mins in 70% of women with severe hypertension and 91% reach target within 130 mins.

Click the I.V. bag to see types of treatment.



Nitroglycerin

A good option for treatment of hypertension associated with pulmonary edema [80].

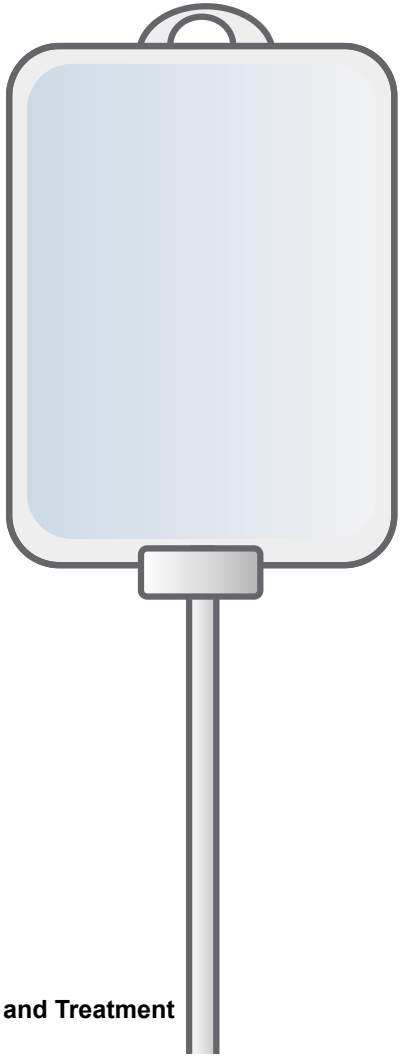
Administer 5mcg/min IV and gradually increase every 3 to 5 minutes to maximum dose of 100mcg/min.

Typically only administered in ICU settings.

Nicardipine

- If IV labetalol, IV hydralazine and PO instant-release nifedipine are not effective in controlling a patient's blood pressure, a nicardipine drip can be started; however, this is typically only managed in an ER or ICU setting.

Click here to see more information.



Rarely is BP not controlled with the drugs discussed previously.

Nitroprusside is administered as a last resort.

Requesting assistance from maternal fetal medicine, anesthesia or critical care may be required if typical antihypertensive management fails.

Maintenance Antihypertensive Therapy

If a woman is diagnosed with pre-eclampsia with severe features based on severe range blood pressure alone (no other severe features are present), she is a candidate for expectant management and should be started on oral antihypertensive therapy.

Options for oral antihypertensive therapy and typical starting doses include:

- Labetalol 200 mg BID
- Nifedipine XL 30 mg daily

Click Here to view a video from ACOG: Failure of Physical Transformation and Spiral Artery Atherosis: Their Role in Preeclampsia

https://www.ajog.org/cms/10.1016/j.ajog.2020.09.026/attachment/e9990ceb-ea6d-4cd9-8b0e-116aaaf56ba5/mmc1.mp4

Target BP

- Systolic 130 to 150mmHg
- Diastolic 80 to 100mmHg

How quickly the BP should be brought to safe levels is controversial.

- Cerebral, myocardial ischemia or infarction can be induced by aggressively reducing the BP.
- It is reasonable to reduce the mean arterial pressure by no more than 25% over two hours and achieving a target of 130-150mmHg systolic and 80-100mmHg diastolic [80].
- Appropriate and prompt management of severe systolic and severe diastolic hypertension is required to reduce risk and have successful, safe clinical outcomes for women with preeclampsia or eclampsia [98].
- There is mounting evidence that patient outcomes improve when standardization of care occurs [98].
- Adverse maternal outcomes have been reduced when introducing standardization of evidence based clinical guidelines for the management of patients with preeclampsia and eclampsia [98].

MAGNESIUM SULFATE

- Given for the prevention and treatment of seizures in women with severe features of preeclampsia and eclampsia.
- A loading dose of 6 grams intravenous over 15-20 minutes followed by 2 grams per hour as a continuous infusion is the most common regimen [82-85].
- An alternative regimen is 5 grams intramuscularly into each buttock (total of 10 grams) followed by 5 grams intramuscularly every 4 hours.
- A clear threshold concentration has not been determined but there is a recommendation based on retrospective data to help insure the prevention of convulsions with a therapeutic range of 4.8 - 8.4mg/dL (2-3.5mmol/L) [86].
- Loading doses less than 6 grams are more likely to result in subtherapeutic magnesium levels (less than 4.5mg/dL) [84,87].

MAGNESIUM SULFATE

- Since magnesium sulfate is excreted by the kidneys, dosing should be adjusted in women with renal insufficiency (defined as a serum creatinine greater than 1.0mg/dL).
- Consideration should be given to administer a 4 gram bolus (rather than 6 gram) and the maintenance rate should be reduced to 1 gram/hour.
- Labs for creatinine and magnesium levels should be followed every 6-12 hours.
- Clinical assessments should be performed hourly.
- The maintenance phase is given only if a patellar reflex is present (loss of reflexes being the first manifestation of symptomatic hypermagnesemia), respirations exceed 12 per minute, and the urine output exceeds 100mL per 4 hours.
- Following serum magnesium levels is not required if the woman's clinical status is closely monitored for evidence of potential magnesium toxicity.
- The maintenance dose should be decreased if there is clinical evidence of magnesium toxicity.

MAGNESIUM SULFATE

Duration of Therapy:

- Magnesium sulfate is typically initiated at the time of diagnosis of preeclampsia with severe features; however, there are no specific guidelines for the duration of therapy if expectant management is planned.
- Continuing the infusion for 12-24 hours after initial diagnosis is typical.
- If a patient has been expectantly managed, magnesium sulfate is restarted whenever delivery is initiated and it is continued for 24 hours postpartum.
- If immediate delivery is planned, magnesium sulfate is started and continued until 24 hours postpartum.
- Diuresis (greater than 4L/day) is believed to be the most accurate clinical indicator of resolution of preeclampsia/eclampsia, but is not a guarantee against the development of seizures [88].

Mechanism of Anticonvulsant Action:

- The mechanism for the anticonvulsant effects of magnesium sulfate has not been clearly defined.
- The primary effect is thought to be central.
- Another theory is that it promotes vasodilatation of constricted cerebral vessels by opposing calcium-dependent arterial vasospasm, thereby reducing cerebral barotrauma [89].

MAGNESIUM SULFATE

Complications and Side Effects:

- Rapid infusion of magnesium sulfate causes diaphoresis, flushing, and warmth, probably related to peripheral vasodilation.
- Nausea, vomiting, headache, muscle weakness, visual disturbances, and palpitations can also occur.
- Dyspnea or chest pain may be symptoms of pulmonary edema, which is a rare side effect.
- Magnesium toxicity is uncommon in women with normal renal function [90].

Toxicity is Related to Serum Magnesium Concentration:

- Loss of DTR occurs at 7 to 10mEq/L (8.5 to 12mg/dL or 3.5 to 5.0mmol/L).
- Respiratory paralysis at 10 to 13mEq/L (12 to 16mg/dL or 5.0 to 6.5mmol/L).
- Cardiac conduction is altered at >15mEq/L (>18mg/dL or >7.5mmol/L).
- Cardiac arrest occurs at >25mEq/L (>30mg/dL or >12.5mmol/L) [150].
- Calcium gluconate (1 gram IV over 5 to 10 minutes) should be administered only to counteract life-threatening symptoms of magnesium toxicity, such as cardiorespiratory compromise.

MAGNESIUM SULFATE

- Magnesium sulfate is contraindicated in women with myasthenia gravis since it can precipitate a severe myasthenic crisis.
- Neuromuscular blockade and hypotension due to concurrent use of magnesium sulfate and calcium channel blockers have been described in case reports, but the risk appears to be minimal [92].
- Although magnesium sulfate is a weak tocolytic, labor duration does not appear to be affected by magnesium sulfate administration [93].
- When a patient is therapeutic on magnesium sulfate and has a seizure, the first recommendation is an additional loading dose of magnesium sulfate 2g IV over five minutes. If she continues to have seizure activity, alternative anti-convulsants should be considered:
  - Lorazepam 4mg IV over 2-5 minutes (repeating in 5-15 min prn) to maximum of 8mg in 12 hours
  - Diazepam 5-10mg IV slosly (repeating Q15 minutes up to 30mg)
  - Midazolam 1-2mg IV (may repeat in 5-10 minutes)
  - Phenytoin 1000mg IV over 20 minutes
  - iInvolvement of the anesthesia team for further options [101]

ACOG | SOGC

First-Line Therapy

- Labetalol
- Nifedipine

Avoiding:

- Angiotensin-converting enzyme inhibitors
- Angiotensin receptor blockers
- Renin inhibitors
- Mineralocorticoid receptor antangonists

Treatment Goal: BP between 120/80 to 160/105mmHg.

Click the grey arrow for more information.

ACOG | SOGC

ACOG Committee Opinion on emergent therapy acute onset of severe hypertension in pregnancy and postpartum recommends treatment when:

- Severe systolic >160mmHg
- Severe diastolic >110mmHg
- Or both

To achieve BP of 140-150/90-100mmHg [81].

ACOG Committee Opinion on acute onset of severe hypertension in pregnancy and postpartum ***recommends first-line treatment with***:

- Labetalol
- Hydralazine
- Oral Nifedipine

Recommend using short-acting preparation of oral nifedipine.

Click the tabs to see recommendations.

ACOG | SOGC

The Society of Obstetricians and Gynaecologists of Canada (SOGC) guidelines recommend ***antihypertensive treatment for new onset:***

- Systolic BP >160mmHg or
- Diastolic BP >110mmHg

Goal BP <160/110mmHg [95].

Click the tabs to see recommendations.

Common Order Set for Severe Hypertension

1. Notify physician if systolic BP measurement is greater than or equal to 160mmHg or if diastolic BP measurement is greater than or equal to 110mmHg.
2. Fetal surveillance if undelivered and fetus is viable.
3. If severe BP elevations persist for 15 minutes or longer administer labetalol 20mg IV over 2 minutes.
4. Repeat BP measurements in 10 minutes and record results.
5. If either BP threshold is still exceeded, administer labetalol 40mg over 2 minutes.
6. If BP is below threshold, continue BP monitoring closely. Repeat BP measurement in 10 minutes and record results.
7. If either BP threshold is still exceeded, administer labetalol 80mg IV over 2 minutes. If BP is below threshold, continue to monitor BP closely.
8. Repeat BP measurement in 10 minutes and record results.
9. If either BP threshold is still exceeded, administer hydralazine 10mg IV over 2 minutes. If BP is below threshold, continue to monitor BP closely.
10. Repeat BP measurement in 10 minutes and record results.
11. If either BP threshold is still exceeded, obtain emergency consultation from Maternal Fetal Medicine (MFM), Internal Medicine (IM), anesthesia or Critical Care subspecialty.
12. Give specific antihypertensive meds per order.
13. Once BP thresholds are achieved repeat BP measurements every 10 minutes for an hour, then every 15 minutes for an hour, then every 30 minutes for an hour, then every hour for 4 hours [96].

Multi-organ involvement may result in fetal, perinatal and maternal morbidity and mortality [97].

Maternal complications include but are not limited to:

- Stroke
- Pulmonary edema
- Hepatic failure
- Jaundice
- Eclampsia

Women developing eclampsia are at great risk for:

- Maternal death
- Need for assisted ventilation
- Adult respiratory distress syndrome (ARDS)
- Embolism
- Placenta abruption
- Acute renal failure [98]
- PRES

Fetal complications

- Oligohydramnios
- Fetal growth restriction
  - Up to 30% of fetus' of women with preeclampsia
- Metabolic acidosis
- APGAR score <3 at 5 minutes
- Umbilical artery pH <7
- Positive pressure ventilation (PPV) for <5 minutes

Delivery Recommendations

- Gestational Hypertension - 37 weeks
- Preeclampsia without severe features - 37 weeks
- Preeclampsia with severe features - 34 weeks

Expectant Management of Preeclampsia

- If a patient is diagnosed with preeclampsia with severe features prior to 34 weeks, expectant management can be employed if the only severe feature is hypertension.
- The patient should be admitted to a facility with capacity to care for both the patient and the neonate
- In these cases, the patient is typically started on magnesium sulfate for 12-24 hours, is given antenatal corticosteroids and can be started on oral antihypertensive medication.
- The patient should undergo frequent vital signs, daily assessment of symptoms, daily fetal monitoring, frequent lab assessment (every 1-7 days) and weekly ultrasounds.
- If the patient and fetus remain stable, delivery is recommended at 34 weeks.

Expectant Management of Preeclampsia

If a patient is admitted for preeclampsia with severe features prior to 34 weeks, delivery is recommended in any of the following scenarios:

- Uncontrolled severe range BP that do not respond to antihypertensive medication
- Persistent headaches, refractory to treatment
- Epigastric pain or right upper quadrant pain unresponsive to pain medication
- Visual disturbances, motor deficit or altered mental status
- Stroke
- Myocardial infarction
- HELLP syndrome
- New or worsening renal dysfunction (creatinine >1.1 or 2x baseline)
- Pulmonary edema
- Eclampsia
- Placental abruption
- Abnormal fetal testing
- Fetal death
- Fetus without expected survival at the time of maternal diagnosis either based on lethal abnormality or previable gestational age
- Persistent reverse end diastolic flow in umbilical artery Dopplers

In a pregnant patient, preeclampsia is the most common cause of:

- Hypertension
- Thrombocytopenia
- Liver abnormalities
- Renal abnormalities

Other health care conditions should be considered and excluded:

- Acute fatty liver of pregnancy (AFLP)
- Thrombotic thrombocytopenic purpura (TTP)
- Systemic Lupus Erythematosus (SLE) exacerbation

The California Maternal Quality Care Collaborative developed a tool to help differentiate between these disorders. It is a free download from their website [101].

Table 5. Differentiation between Preeclampsia, HELLP Syndrome, Acute Fatty Liver Disease of Pregnancy (AFLD), Thrombotic Thrombocytopenia Purpura (TTP), Hemolytic Uremia Syndrome (HUS) *

	Plts	LFTs	Bili	Cr	LDH	Glu	DIC	CNS
Preeclampsia	±	±	±	±	±	→	±	±
HELLP	↓/↓↓	↑↑	↑	±	↑	→	±	±
AFLD	↓↓	↑↑	↑↑↑	↑	↑	↓↓↓	↑↑↑	±
TTP	↓↓↓	↑	↑	↑	↑↑	→	±	++
HUS	↓	↑↑	↑↑	↑↑↑	↑	→	±	±

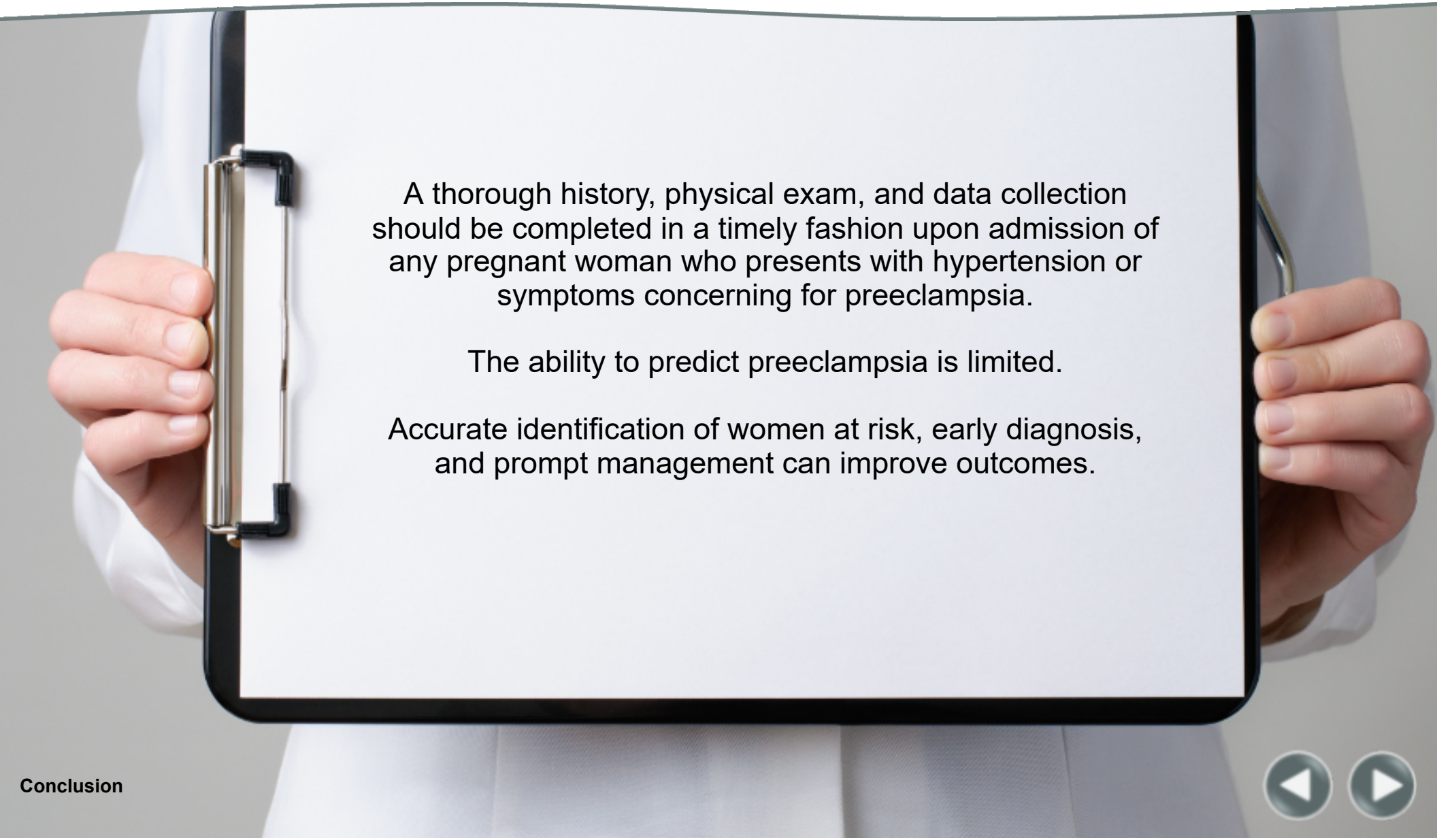
AFLD: Acute Fatty Liver Disease of Pregnancy; TTP: Thrombotic Thrombocytopenic Purpura; HUS: Hemolytic Uremia Syndrome; Plts: platelet count; LFTs: liver function test; Bili: total bilirubin level; LDH: Lactate Dehydrogenase; Glu: glucose; DIC: Disseminated Intravascular Coagulation; CNS: Central Nervous System symptoms (confusion, visual changes, headache)

*Arrows represent relative changes: one arrow equals some increase; two arrows indicate moderate increase, and three arrows equal very high increase.

Lyndon A, Lagrew D, Shields L, Main E, Cape V. Improving Health Care Response to Obstetric Hemorrhage. (California Maternal Quality Care Collaborative Toolkit to Transform Maternity Care) Developed under contract #11-10006 with the California Department of Public Health; Maternal, Child and Adolescent Health Division; Published by the California Maternal Quality Care Collaborative, 3/17/15. Reprinted with permission.

Another issue with maternal morbidity and mortality arises from lack of communication. Misdiagnosis and denial of severity of women's illness along with delays or failures in treatment are key factors contributing to fatal outcomes. Lack of listening skills or responsiveness to concern and failure in communication including silence in the face of clinical concern are likely to have contributed to delays, misdiagnosis, and treatment failures.

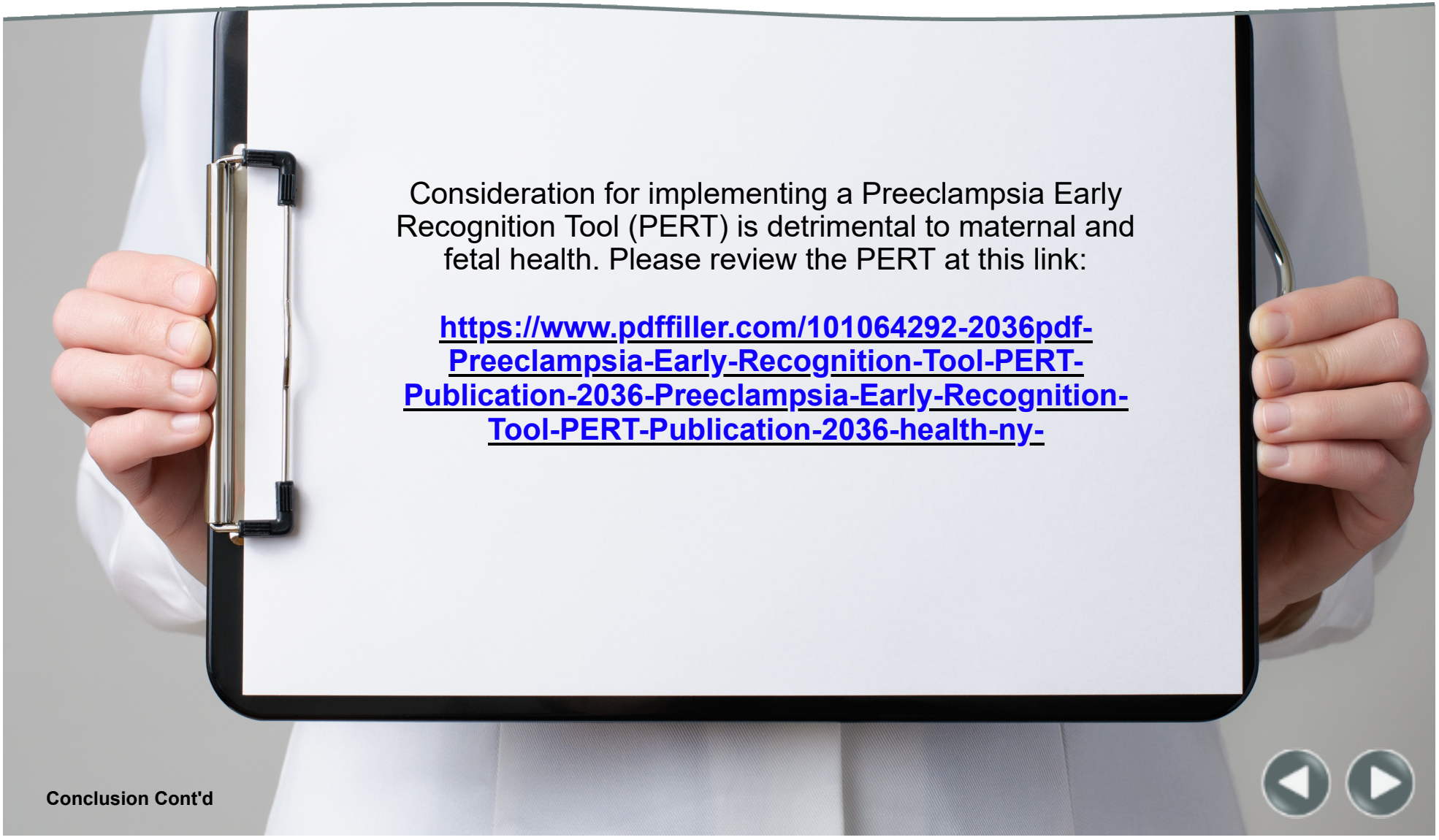
Teams are found to be effective with collective monitoring, crosschecking one another, and clinical processes in place to proactively identify potential problems. Empowering all staff to "stop the line" or formally interrupt the plan of care and check safety when they observe potential for harm. Listening to a peer whether or not they agree and establishing strategies for communication and teamwork will help to build trust in these complex settings [101].



A thorough history, physical exam, and data collection should be completed in a timely fashion upon admission of any pregnant woman who presents with hypertension or symptoms concerning for preeclampsia.

The ability to predict preeclampsia is limited.

Accurate identification of women at risk, early diagnosis, and prompt management can improve outcomes.


Consideration for implementing a Preeclampsia Early Recognition Tool (PERT) is detrimental to maternal and fetal health. Please review the PERT at this link:
https://www.pdffiller.com/101064292-2036pdf-Preeclampsia-Early-Recognition-Tool-PERT-Publication-2036-Preeclampsia-Early-Recognition-Tool-PERT-Publication-2036-health-ny-
Conclusion Cont'd

Congratulations!

You have successfully completed this module.

Click on the above 'X' to take the post-test for this course.
If you do not attain a passing score after two attempts at the post-test the entire program must be repurchased.

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