Hypertensive disorders of pregnancy

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References

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- ACOG Guidelines #202, 2019
- Leeman et al. Am Fam Physician. 2016 Jan 15;93(2):121-127
- Poon et al, 2019. The International Federation of Gynecology and Obstetrics (FIGO) initiative on pre-eclampsia: A pragmatic guide for first-trimester screening and prevention

OUTLINE

- 4 Types of hypertensive disorders in pregnancy
- Diagnosis
- Risk factors
- Etiopathogenesis
- Prevention
- Treatment

Four types of hypertensive disorders in pregnancy:

- Gestational hypertension—evidence for the preeclampsia syndrome does not develop and hypertension resolves by 12 weeks postpartum
- Preeclampsia and eclampsia syndrome
- Chronic hypertension of any etiology
- Preeclampsia superimposed on chronic hypertension

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Diagnosis of Hypertensive Disorders

- Hypertension: BP ≥ 140/90
- Korotkoff phase V is used to define diastolic pressure.
- A sudden rise in mean arterial pressure later in pregnancy—"**delta hypertension**"—may also signify preeclampsia even if blood pressure is < 140/90 mm Hg

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

1. Gestational Hypertension

- BP ≥140/90 mm Hg for the first time after midpregnancy, but with **NO proteinuria**
- Almost half of these women subsequently develop preeclampsia syndrome
- reclassified by some as "transient hypertension" if evidence for preeclampsia does not develop and the blood pressure returns to normal by 12 weeks postpartum.

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018 chap 40 Hypertensive disorders

2. Preeclampsia Syndrome

- pregnancy-specific syndrome that can affect virtually every organ system
- Hypertension + proteinuria
- proteinuria is an objective marker and reflects the system-wide endothelial leak
  1. *24-hour urinary excretion > 300 mg;*
  2. *urine protein:creatinine ratio ≥ 0.3;*
  3. *persistent 30 mg/dL (1+ dipstick) protein in random urine samples*
- Evidence of multiorgan involvement may include thrombocytopenia, renal dysfunction, hepatocellular necrosis ("liver dysfunction"), central nervous system perturbations, or pulmonary edema.

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TABLE 40-1. Classification and Diagnosis of Pregnancy-Associated Hypertension

Condition	Criteria Required
Gestational hypertension	BP >140/90 mm Hg after 20 weeks in previously normotensive women
Preeclampsia: Hypertension plus	
Proteinuria	• ≥300 mg/24 h, or • Urine protein: creatinine ratio ≥0.3, or • Dipstick 1+ persistent[a]
	or
Thrombocytopenia	• Platelet count <100,000/μL
Renal insufficiency	• Creatinine level >1.1 mg/dL or doubling of baseline[b]
Liver involvement	• Serum transaminase levels[c] twice normal
Cerebral symptoms	• Headache, visual disturbances, convulsions
Pulmonary edema	—

[a]Recommended only if sole available test.
[b]No prior renal disease.
[c]AST (aspartate transaminase) or ALT (alanine transaminase).
BP = blood pressure.
Modified with permission from American College of Obstetricians and Gynecologists; Task Force on Hypertension in Pregnancy: Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy, Obstet Gynecol. 2013 Nov;122(5):1122–31

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Urine dipstick

2. Preeclampsia Syndrome

- Indicators of Preeclampsia Severity

TABLE 40-2. Indicators of Severity of Gestational Hypertensive Disorders[a]

Abnormality	Nonsevere[b]	Severe
Diastolic BP	<110 mm Hg	≥110 mm Hg
Systolic BP	<160 mm Hg	≥160 mm Hg
Proteinuria[c]	None to positive	None to positive
Headache	Absent	Present
Visual disturbances	Absent	Present
Upper abdominal pain	Absent	Present
Oliguria	Absent	Present
Convulsion (eclampsia)	Absent	Present
Serum creatinine	Normal	Elevated
Thrombocytopenia (<100,000/μL)	Absent	Present
Serum transaminase elevation	Minimal	Marked
Fetal-growth restriction	Absent	Present
Pulmonary edema	Absent	Present
Gestational age	Late	Early

[a]Compare with criteria in Table 40-1.
[b]Includes "mild" and "moderate" hypertension not specifically defined.
[c]Most disregard degrees of proteinuria to classify nonsevere or severe.
BP = blood pressure.

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Eclampsia

- In a woman with preeclampsia, a convulsion that cannot be attributed to another cause is termed ‘eclampsia’.
- the seizures are generalized and may appear before, during, or after labor.

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William’s Obstetrics 24th edition; 2014; chap 40 Hypertensive disorders

Preeclampsia Superimposed on Chronic Hypertension

- Chronic underlying hypertension is diagnosed in women with BP ≥ 140/90 mm Hg before pregnancy or before 20 weeks' gestation, or both.
- If new-onset or worsening baseline hypertension is accompanied by new-onset proteinuria or other findings, then 'superimposed preeclampsia' is diagnosed.
- Compared with "pure" preeclampsia, superimposed preeclampsia commonly develops earlier in pregnancy.
- often is accompanied by fetal-growth restriction.

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

RISK FACTORS

1. Young and nulliparous women (vulnerable to developing preeclampsia)
2. older women (greater risk for chronic hypertension with superimposed preeclampsia)
3. Race, ethnicity, environmental, socioeconomic
4. other risk factors associated with preeclampsia include obesity, multifetal gestation, maternal age, hyperhomocysteinemia, and metabolic syndrome
5. History of preeclampsia

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RISK FACTORS

Box 1. Risk Factors for Preeclampsia

Nulliparity
Multifetal gestations
Preeclampsia in a previous pregnancy
Chronic hypertension
Pregestational diabetes
Gestational diabetes
Thrombophilia
Systemic lupus erythematosus
Prepregnancy body mass index greater than 30
Antiphospholipid antibody syndrome
Maternal age 35 years or older
Kidney disease
Assisted reproductive technology
Obstructive sleep apnea

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ETIOPATHOGENESIS

Hypertensive disorders in pregnancy are more likely to develop in women with the following characteristics:

1. Are exposed to chorionic villi for the first time
2. Are exposed to a superabundance of chorionic villi, as with twins or hydatidiform mole
3. Have preexisting conditions of endothelial cell activation or inflammation such as diabetes or renal or cardiovascular disease
4. Are genetically predisposed to hypertension developing during pregnancy.

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ETIOPATHOGENESIS

- **A fetus is not a requisite for preeclampsia to develop**.
- Presence of chorionic villi is essential, but need not be intrauterine.
- preeclampsia syndrome is characterized by abnormalities that result in vascular endothelial damage with resultant *vasospasm, transudation of plasma, and ischemic and thrombotic sequelae*.

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Etiology

An imposing number of mechanisms have been proposed to explain cause of eclampsia.:

1. Placental implantation with abnormal trophoblastic invasion of uterine vessels
2. Immunological maladaptive tolerance between maternal, paternal (placental), and fetal tissues
3. Maternal maladaptation to cardiovascular or inflammatory changes of normal pregnancy
4. Genetic factors including inherited predisposing genes and epigenetic influences.

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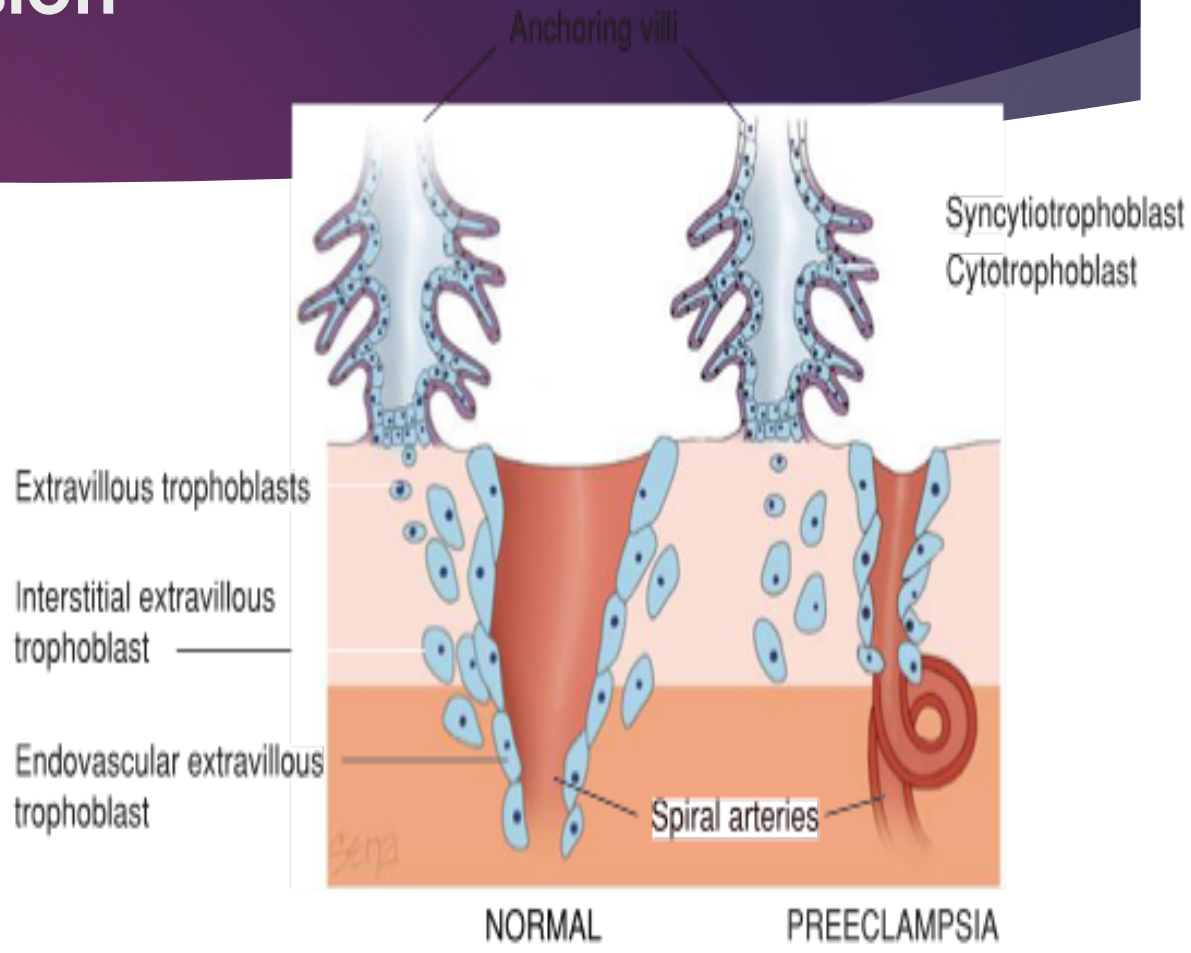
Abnormal Trophoblastic Invasion

- Normal implantation is characterized by extensive remodeling of the spiral arterioles within the decidua basalis
- Endovascular trophoblasts replace the vascular endothelial and muscular linings to enlarge the vessel diameter.



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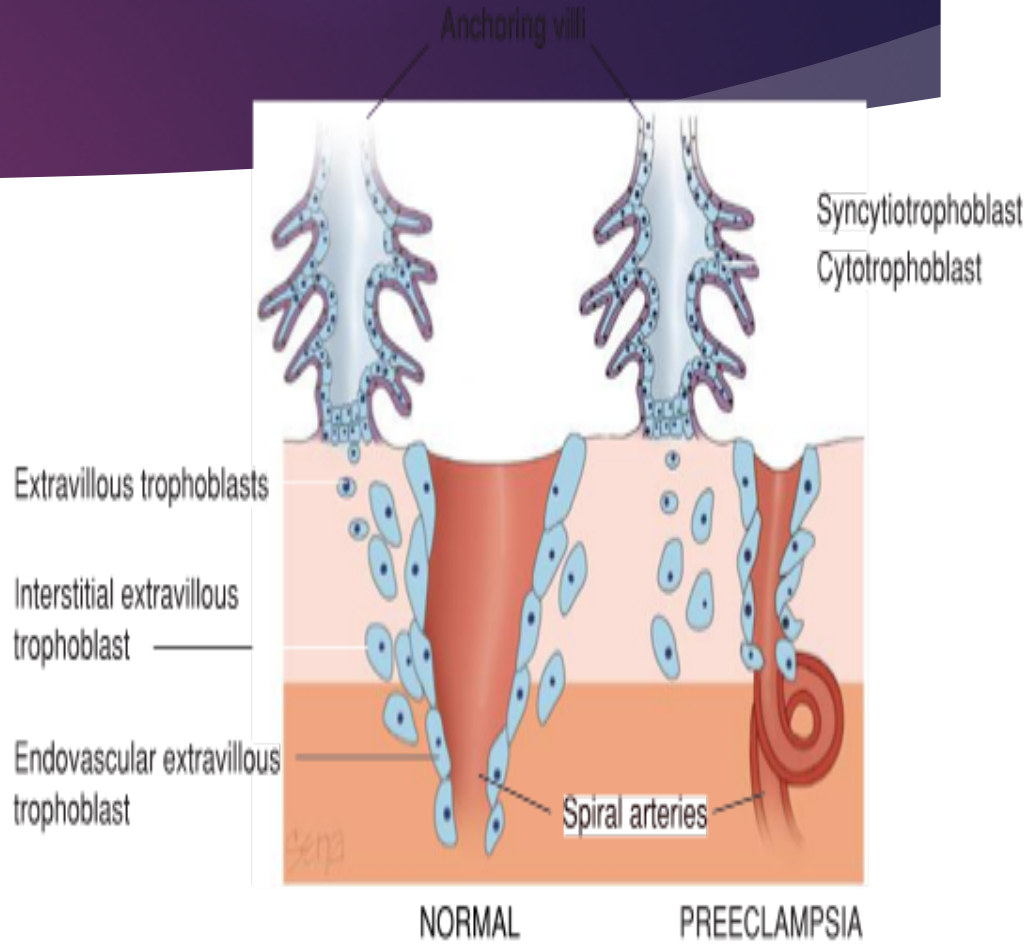
Abnormal Trophoblastic Invasion

- In preeclampsia, there may be incomplete trophoblastic invasion.
- the deeper myometrial arterioles do not lose their endothelial lining and musculoelastic tissue, and their mean external diameter is only half that of corresponding vessels in normal placentas
- In general, the magnitude of defective trophoblastic invasion is thought to correlate with severity of the hypertensive disorder



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Immunological Factors

- Loss of maternal immune tolerance to paternally-derived placental and fetal antigens
- Preeclampsia may be an immune-mediated disorder.
  - For example, the risk of preeclampsia is appreciably enhanced in circumstances in which formation of blocking antibodies to placental antigenic sites might be impaired → the first pregnancy would carry a higher risk.
- In women destined to be preeclamptic, extravillous trophoblasts early in pregnancy express reduced amounts of immunosuppressive nonclassic HLA G.

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Endothelial Cell Activation

- antiangiogenic and metabolic factors and other inflammatory mediators are thought to provoke endothelial cell injury.
- Endothelial cell dysfunction may result from an extreme activated state of leukocytes in the maternal circulation
- cytokines such as tumor necrosis factor-α (TNF-α) and the interleukins (IL) may contribute to the oxidative stress associated with preeclampsia.
- activation of microvascular coagulation manifest by thrombocytopenia; and increased capillary permeability manifest by edema and proteinuria.

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Genetic factors

- preeclampsia is a multifactorial, polygenic disorder.
- incident risk for preeclampsia:
  - 20 to 40 percent for daughters of preeclamptic mothers
  - 11 to 37 percent for sisters of preeclamptic women
  - 22 to 47 percent for twins
- hereditary predisposition for preeclampsia likely is the result of interactions of literally hundreds of inherited genes— both maternal and paternal—that control myriad enzymatic and metabolic functions throughout every organ system.

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Pathogenesis: vasospasm

- Endothelial activation causes vascular constriction with increased resistance and subsequent hypertension.
- Endothelial cell damage causes interstitial leakage through which blood constituents, including platelets and fibrinogen, are deposited subendothelialy
- with diminished blood flow because of maldistribution, ischemia of the surrounding tissues can lead to necrosis, hemorrhage, and other end-organ disturbances characteristic of the syndrome.

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PATHOGENESIS: ENDOTHELIAL CELL INJURY

- Endothelial cell injury has become the centerpiece in the contemporary understanding of preeclampsia pathogenesis
- Protein factor(s)—likely placental—are secreted into the maternal circulation and provoke activation and dysfunction of the vascular endothelium.
- Many of the facets of the clinical syndrome of preeclampsia are thought to result from these widespread endothelial cell changes.
- Intact endothelium has anticoagulant properties, and endothelial cells blunt the response of vascular smooth muscle to agonists by releasing nitric oxide.
  - *Damaged or activated endothelial cells may produce less nitric oxide and secrete substances that promote coagulation and increase sensitivity to vasopressors*

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Pathophysiology: cardiovascular system

- Severe disturbances of normal cardiovascular function are common with preeclampsia syndrome, due to:

1. increased cardiac afterload caused by hypertension
2. cardiac preload, which is affected negatively by pathologically diminished hypervolemia of pregnancy and is increased by intravenous crystalloid or oncotic solutions
3. endothelial activation with interendothelial extravasation of intravascular fluid into the extracellular space and importantly, into the lungs

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Pathophysiology: cardiovascular system

- With the clinical onset of preeclampsia, cardiac output declines, due to increased peripheral resistance.
- (+) hyperdynamic ventricular function, elevated pulmonary capillary wedge pressures:
  1. pulmonary edema may develop despite normal ventricular function because of an alveolar endothelial-epithelial leak
  2. aggressive fluid administration substantially elevates normal left-sided filling pressures and increases a physiologically normal cardiac output to hyperdynamic levels.

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Pathophysiology: cardiovascular system

- (**+) hemoconcentration** - results from generalized vasoconstriction that follows endothelial activation and leakage of plasma into the interstitial space because of increased permeability (lower blood volume than normal pregnant women)
- Women with eclampsia:
  - Are unduly sensitive to vigorous fluid therapy administered in an attempt to expand the contracted blood volume to normal pregnancy levels
  - Are sensitive to amounts of blood loss at delivery that are considered normal for a normotensive woman.

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Pathophysiology: hematologic changes

THROMBOCYTOPENIA

- **Overt thrombocytopenia** - platelet count < 100,000/μL—indicates severe disease
- the lower the platelet count, the higher the rates of maternal and fetal morbidity and mortality
- In most cases, delivery is advisable because thrombocytopenia usually continues to worsen.
- After delivery, the platelet count may continue to decline for the first day or so → increases progressively to reach a normal level within 3 to 5 days.

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Pathophysiology: hematologic changes

HEMOLYSIS

- manifested by elevated serum lactate dehydrogenase levels and decreased haptoglobin levels.
- Other evidence comes from schizocytosis, spherocytosis, and reticulocytosis in peripheral blood
- result from microangiopathic hemolysis caused by endothelial disruption with platelet adherence and fibrin deposition.
- Erythrocytic membrane changes, increased adhesiveness, and aggregation may also promote a hypercoagulable state

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Pathophysiology: hematologic changes

HELLP SYNDROME

- **H**EMOLYSIS, **E**LEVATED **L**IVER ENZYMES, **L**OW **P**LATELET COUNT
- abnormally elevated serum liver transaminase levels are indicative of hepatocellular necrosis
- included in criteria that differentiate severe from nonsevere preeclampsia.
- **Complete or Partial HELLP** *(one or two but not all three of the laboratory findings.)*

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Diagnostic Criteria for HELLP Syndrome

Alanine or aspartate transaminase levels ≥ 2 times upper limit of normal

Hemolysis

- Lactate dehydrogenase > 600 U per L (10.0 µkat per L)
- Peripheral blood smear shows evidence of damaged erythrocytes (e.g., schistocytes, burr cells, helmet cells)
- Serum bilirubin ≥ 1.2 mg per dL (20.5 µmol per L)

Platelet count < 100×10^3 per µL (100×10^9 per L)

Leeman et al. Am Fam Physician. 2016 Jan 15;93(2):121-127

Pathophysiology: Fluid and Electrolyte Changes

- In women with severe preeclampsia, the volume of extracellular fluid, manifest as edema → greater than that in normal pregnant women.
- the mechanism responsible for pathological fluid retention is thought to be endothelial injury
- plasma oncotic pressure → creates a filtration imbalance and further displaces intravascular fluid into the surrounding interstitium.
- Following an eclamptic convulsion, the serum pH and bicarbonate concentration are lowered due to lactic acidosis and compensatory respiratory loss of carbon dioxide..

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Pathophysiology: kidney

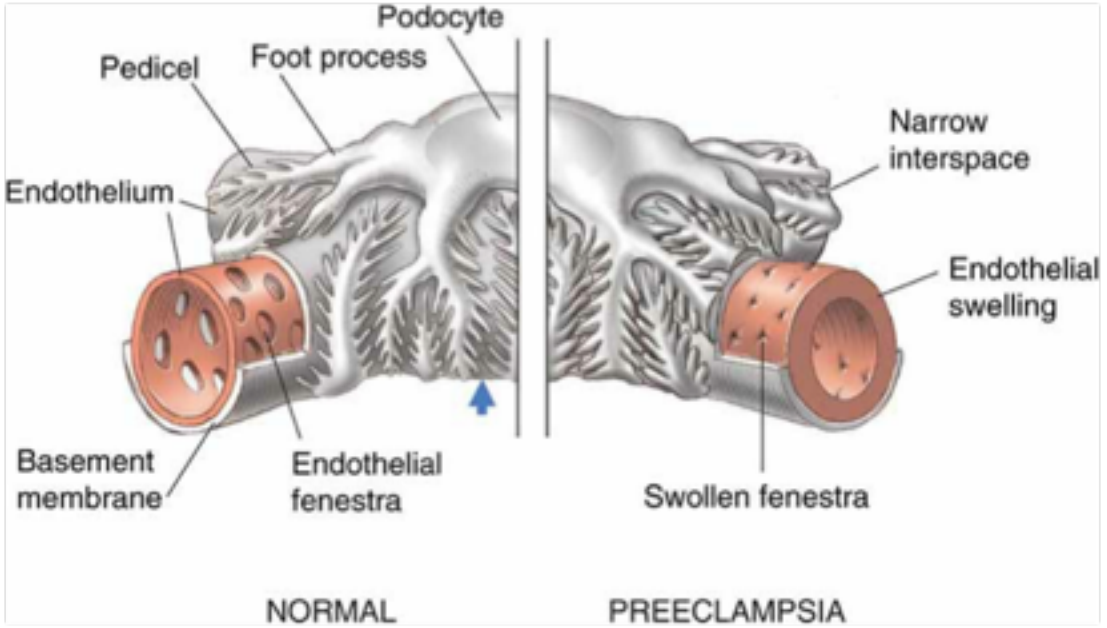

FIGURE 40-7 Schematic showing glomerular capillary endotheliosis. The capillary of the normal glomerulus shown on the left has wide endothelial fenestrations, and the pedicels emanating from the podocytes are widely spaced (*arrow*). The illustration on the right is of a glomerulus with changes induced by the preeclampsia syndrome. The endothelial cells are swollen and their fenestrae narrowed, as are the pedicels that now abut each other.

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Pathophysiology: kidney

- renal perfusion and glomerular filtration are reduced.
- decreased glomerular filtration may result from reduced plasma volume. Most of the decrement, however, is from increased renal afferent arteriolar resistance that may be elevated up to 5 fold → OLIGURIA
- *Intensive intravenous fluid therapy is not indicated* as "treatment" for preeclamptic women with oliguria, as rapid infusions may cause clinically apparent pulmonary edema.

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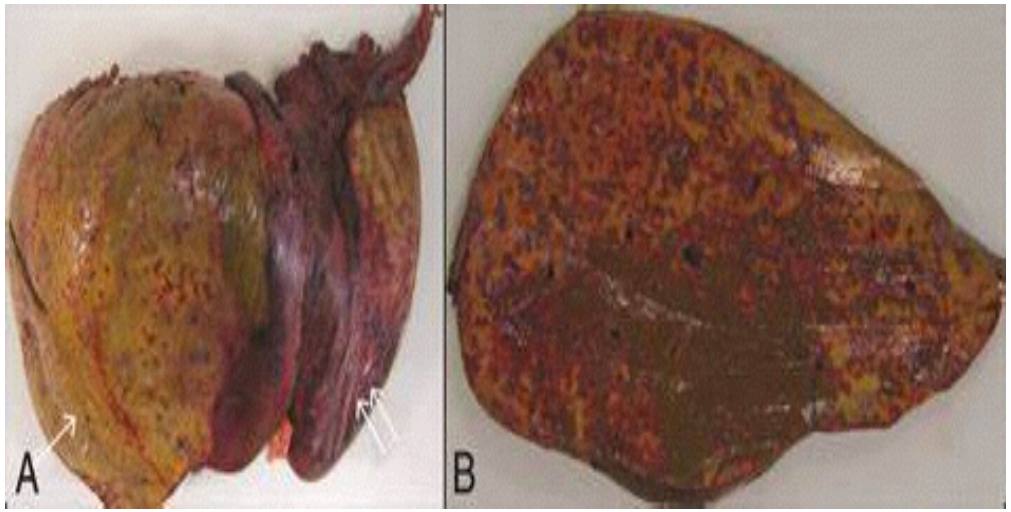
Pathophysiology: LIVER

- Severe preeclampsia may manifest with moderate to severe right-upper quadrant or midepigastric pain and tenderness, secondary to hepatocellular infarction/hemorrhagic necrosis, hepatic cell edema, or Glisson's capsule distension, or a combination, or rarely liver hematomas.



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Pathophysiology: Neurological Manifestations

- Severe preeclampsia may manifest with headache and scotomata and are thought to arise from cerebrovascular hyperperfusion that has a predilection for the occipital lobes.
- 20 to 30 % have visual changes preceding eclamptic convulsions.
- headaches may be mild to severe and do not usually respond to traditional analgesia, but they do improve after magnesium sulfate infusion is initiated.
- Convulsions are a second potential manifestation and are diagnostic for eclampsia → caused by *excessive release of excitatory neurotransmitters*—especially glutamate; massive depolarization of network neurons; and bursts of action potentials

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Pathophysiology: Neurological Manifestations

- blindness is rare with preeclampsia alone, but it complicates eclamptic convulsions in up to 15 percent of women.
- usually improve with magnesium sulfate therapy and/or lowered blood pressure.
- is usually reversible, and may arise from three potential areas: visual cortex of the occipital lobe, the lateral geniculate nuclei, and the retina.
  - *Occipital blindness is also called **"amaurosis"—** Affected women usually have evidence of extensive occipital lobe vasogenic edema on imaging studies.*
  - *occipital blindness lasted from 4 hours to 8 days, but it resolves completely*
  - *Rarely, extensive cerebral infarctions may result in total or partial visual defects*

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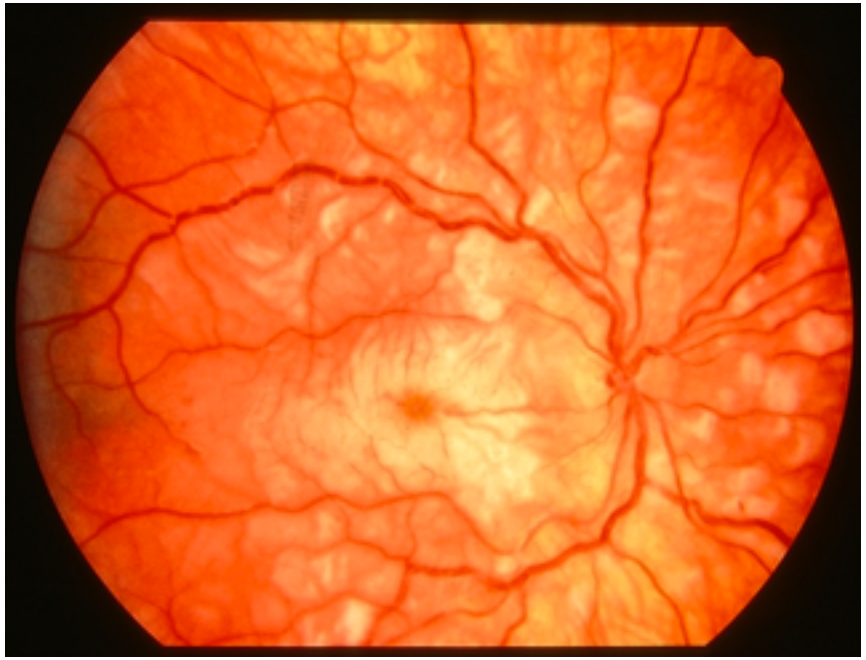
Pathophysiology: Neurological Manifestations

- Blindness from retinal lesions is caused either by serous retinal detachment or rarely by retinal infarction, which is termed **Purtscher retinopathy**
- Serious retinal detachment is usually unilateral and seldom causes total visual loss.



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Pathophysiology: Neurological Manifestations

- generalized cerebral edema may develop and is usually manifest by mental status changes that vary from confusion to coma. → dangerous because fatal transtentorial herniation may result.

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Prediction and prevention

TABLE 40-5. Predictive Tests for Development of the Preeclampsia Syndrome

Testing Related To:	Examples
Placental perfusion/vascular resistance	Roll-over test, isometric handgrip or cold pressor test, pressor response to aerobic exercise, angiotensin-II infusion, midtrimester mean arterial pressure, platelet angiotensin-II binding, renin, 24-hour ambulatory blood pressure monitoring, uterine artery or fetal transcranial Doppler velocimetry
Fetal-placental unit endocrine dysfunction	Human chorionic gonadotropin (hCG), alpha-fetoprotein (AFP), estriol, pregnancy-associated protein A (PAPP A), inhibin A, activin A, placental protein 13, procalcitonin, corticotropin-releasing hormone, A disintegrin, ADAM-12, kisspeptin
Renal dysfunction	Serum uric acid, microalbuminuria, urinary calcium or kallikrein, microtransferrinuria, *N*-acetyl-β-glucosaminidase, cystatin C, podocyturia, podocalyxin
Endothelial dysfunction/ oxidant stress	Platelet count and activation, fibronectin, endothelial adhesion molecules, prostaglandins, prostacyclin, MMP-9, thromboxane, C-reactive protein, cytokines, endothelin, neurokinin B, homocysteine, lipids, insulin resistance, resistin, antiphospholipid antibodies, plasminogen activator-inhibitor (PAI), leptin, p-selectin, angiogenic and antiangiogenic factors such as placental growth factor (PlGF), vascular endothelial growth factor (VEGF), fms-like tyrosine kinase receptor-1 (sFlt-1), endoglin
Others	Antithrombin-III(AT-3), atrial natriuretic peptide (ANP), β_2-microglobulin, haptoglobin, transferrin, ferritin, 25-hydroxyvitamin D, genetic markers, cell-free fetal DNA, serum and urine proteomics and metabolomic markers, hepatic aminotransferases

ADAM12 = ADAM metallopeptidase domain 12; MMP = matrix metalloproteinase.
Adapted from Conde-Agudelo, 2015, Duckworth, 2016.

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Prediction and prevention: vascular resistance testing

Provocative Pressor Tests.

- Three tests have been extensively evaluated to assess the blood pressure rise in response to a stimulus:
  - **Roll-over test** measures the hypertensive response in women at 28 to 32 weeks who are resting in the left lateral decubitus position and then roll over to the supine position.
    - Increased blood pressure signifies a positive test.
  - **Isometric exercise test** employs the same principle by squeezing a handball.
  - **Angiotensin II infusion test** is performed by giving incrementally increasing doses intravenously, and the hypertensive response is quantified.

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Prediction and prevention: vascular resistance testing

Uterine Artery Doppler Velocimetry

- Faulty trophoblastic invasion of the spiral arteries, results in diminished placental perfusion and upstream increased uterine artery resistance.
- Increased uterine artery velocimetry determined by Doppler ultrasound in the first two trimesters should provide indirect evidence of this process and thus serve as a predictive test for preeclampsia
- increased flow resistance results in an abnormal waveform represented by an exaggerated diastolic notch.

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Prevention

- Some Methods to Prevent Preeclampsia That Have Been Evaluated in Randomized Trials:

- Dietary manipulation—low-salt diet, calcium or fish oil supplementation
- Exercise—physical activity, stretching
- Cardiovascular drugs—diuretics, antihypertensive drugs
- Antioxidants—ascorbic acid (vitamin C), α-tocopherol (vitamin E), vitamin D
- Antithrombotic drugs—low-dose aspirin, aspirin/dipyridamole, aspirin + heparin, aspirin + ketanserin

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

PREVENTION OF PREECLAMPSIA

- Following the first-trimester screening and assessment for preterm PE, women identified at high risk should receive aspirin prophylaxis commencing at 11–14 weeks of gestation at a dose of 150 mg to be taken every night until either 36 weeks of gestation, when delivery occurs, or when PE is diagnosed.

Poon et al, 2019. The International Federation of Gynecology and Obstetrics (FIGO) initiative on pre-eclampsia: A pragmatic guide for first-trimester screening and prevention

PREVENTION OF PREECLAMPSIA

Table 1. Clinical Risk Factors and Aspirin Use*

Level of Risk	Risk Factors	Recommendation
High†	• History of preeclampsia, especially when accompanied by an adverse outcome • Multifetal gestation • Chronic hypertension • Type 1 or 2 diabetes • Renal disease • Autoimmune disease (ie, systemic lupus erythematosus, the antiphospholipid syndrome)	Recommend low-dose aspirin if the patient has one or more of these high-risk factors
Moderate‡	• Nulliparity • Obesity (body mass index greater than 30) • Family history of preeclampsia (mother or sister) • Sociodemographic characteristics (African American race, low socioeconomic status) • Age 35 years or older • Personal history factors (eg, low birth weight or small for gestational age, previous adverse pregnancy outcome, more than 10-year pregnancy interval)	Consider low-dose aspirin if the patient has more than one of these moderate-risk factors§
Low	• Previous uncomplicated full-term delivery	Do not recommend low-dose aspirin

ACOG Practice Bulletin #202, 2019

Proposed aspirin regimen for preterm preeclampsia

Maternal weight, kg	Daily required dosage, mg	Administration, mg
<40	100	1 × 100
≥40	~150	2 × 60 2 × 75 2 × 81 1 × 100 + ½ × 100 (discard the other half) ½ × 300 (discard the other half)

Poon et al, 2019. The International Federation of Gynecology and Obstetrics (FIGO) initiative on pre-eclampsia: A pragmatic guide for first-trimester screening and prevention

Management

- management varies with the severity of endothelial cell injury and multiorgan dysfunction.
- Increased surveillance permits more prompt recognition of ominous changes in blood pressure, critical laboratory findings, and clinical signs and symptoms
- basic management objectives for any pregnancy complicated by preeclampsia are:
  - *(1) termination of pregnancy with the least possible trauma to mother and fetus*
  - *(2) birth of an infant who subsequently thrives*
  - *(3) complete restoration of health to the mother*

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Management : evaluation

A systematic evaluation is instituted to include the following:

1. Detailed examination, which is followed by daily scrutiny for clinical findings such as headache, visual disturbances, epigastric pain, and rapid weight gain
2. Weight determined daily
3. Analysis for proteinuria or urine protein:creatinine ratio
4. Blood pressure readings
5. serum creatinine, complete blood count with platelet, liver enzymes
6. Evaluation of fetal size and well-being and amnionic fluid volume

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Goals of management

1. early identification of worsening preeclampsia
2. development of a management plan for timely delivery.

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Consideration for Delivery

- **Termination of pregnancy** is the *only cure* for preeclampsia.
- Headache, visual disturbances, oliguria, and epigastric pain are ominous signs. (may be indicative that convulsions may be imminent)
- Severe preeclampsia demands anticonvulsant and antihypertensive therapy, followed by delivery.
- Goals of treatment are to forestall convulsions, to prevent intracranial hemorrhage and serious damage to other vital organs, and to deliver a healthy newborn.

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Consideration for delivery

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Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Consideration for delivery

- With moderate or severe preeclampsia that does not improve after hospitalization, delivery is advisable for the welfare of both mother and fetus.
  - Labor induction is carried out, usually with preinduction cervical ripening from a prostaglandin or osmotic dilator
  - Whenever it appears that induction almost certainly will not succeed or attempts have failed, then cesarean delivery is indicated.

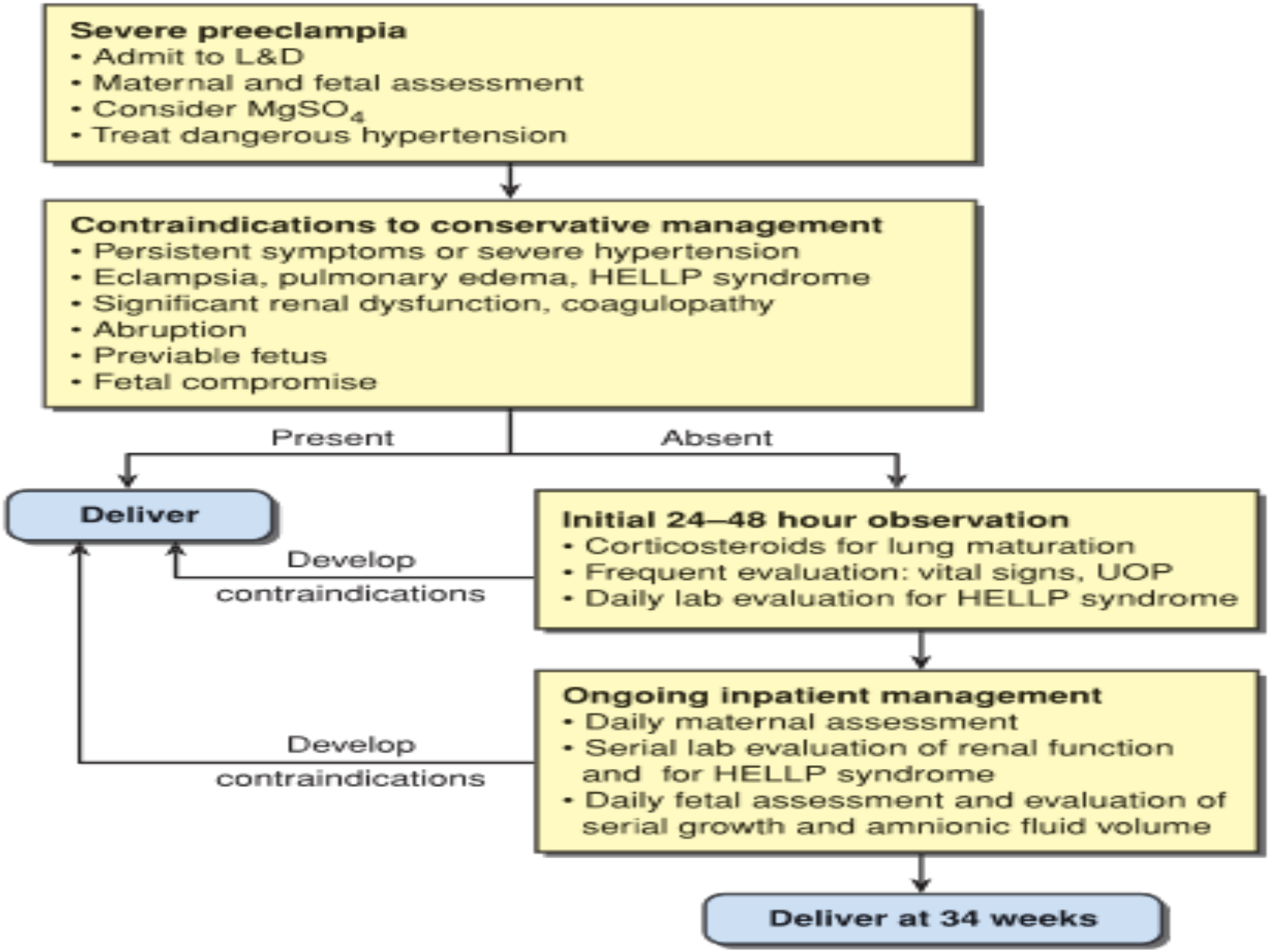
Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Glucocorticoids for Lung Maturation

- Glucocorticoids have been administered to women with severe hypertension who are remote from term.
- Treatment does not seem to worsen maternal hypertension, and a decrease in the incidence of respiratory distress and improved fetal survival has been noted.
- Neonatal complications, including respiratory distress, intraventricular hemorrhage, and death, were decreased significantly when betamethasone was given compared with placebo.

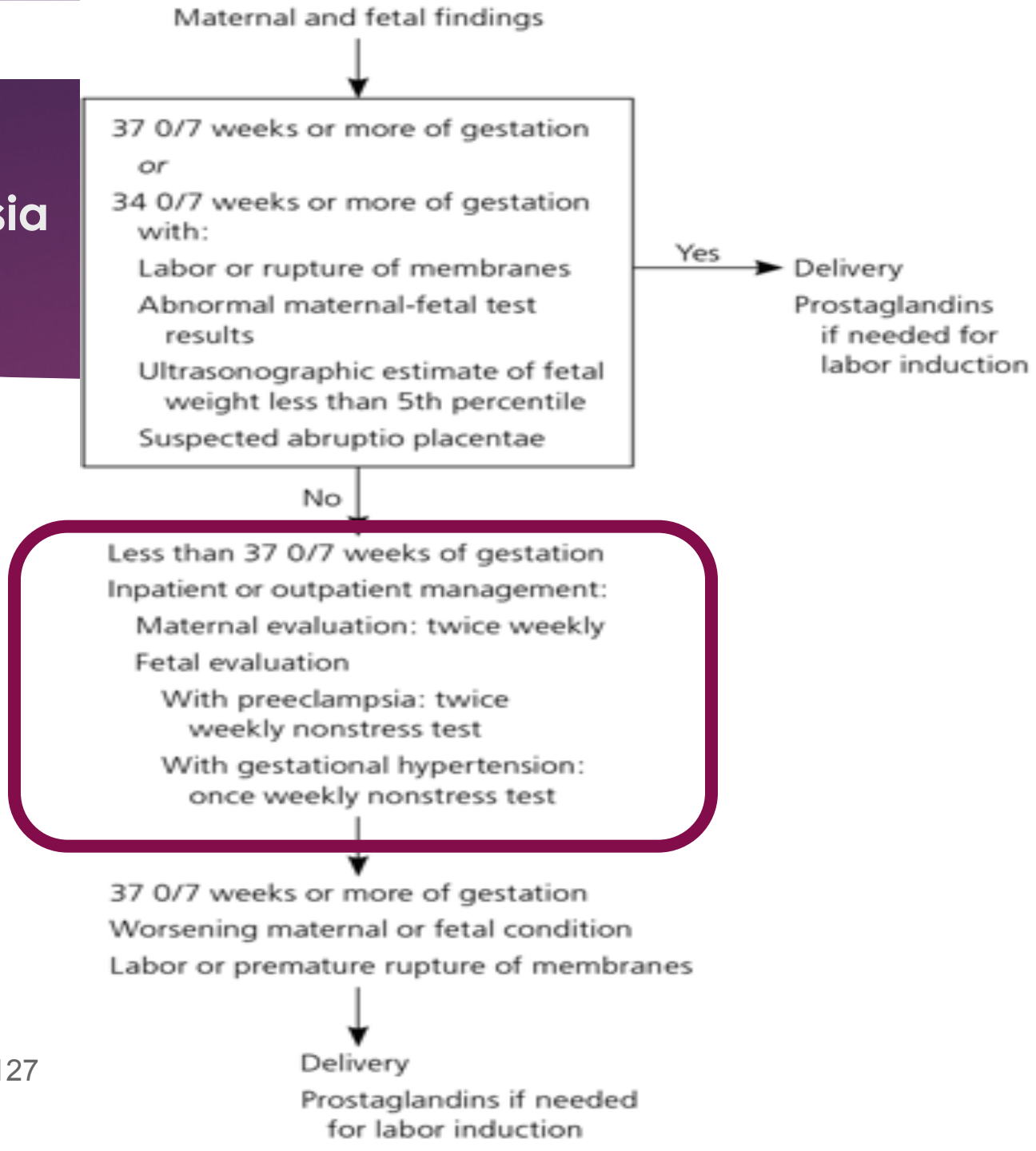
Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Management algorithm for severe preeclampsia < 34 weeks



Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Management of Gestational Hypertension and Preeclampsia Without Severe Features



Leeman et al. Am Fam Physician. 2016 Jan 15;93(2):121-127

Indications for delivery in severe preeclampsia < 34 weeks

Corticosteroid Therapy for Lung Maturation[a] and Delivery after Maternal Stabilization:

- Uncontrolled severe hypertension
- Eclampsia
- Pulmonary edema
- Placental abruption
- Disseminated intravascular coagulation
- Nonreassuring fetal status
- Fetal demise

Corticosteroid Therapy for Lung Maturation—Delay Delivery 48 hr If Possible:

- Preterm ruptured membranes or labor
- Thrombocytopenia < 100,000/μL
- Hepatic transaminase levels twice upper limit of normal
- Fetal-growth restriction
- Oligohydramnios
- Reversed end-diastolic Doppler flow in umbilical artery
- Worsening renal dysfunction

[a]Initial dose only, do not delay delivery.
From the Society for Maternal-Fetal Medicine, 2011, and the Task Force of the American College of Obstetricians and Gynecologists, 2013b.

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 24th edition; 2014; chap 40 Hypertensive disorders

Management of Eclampsia

- Magnesium sulfate is highly effective in preventing convulsions in women with preeclampsia and in stopping them in those with eclampsia.
- Tenets of management of eclampsia
  1. Control of convulsions using an IV loading dose of magnesium sulfate, followed by a maintenance dose, usually intravenous.
  2. Intermittent administration of an antihypertensive medication to lower blood pressure
  3. Avoidance of diuretics unless there is obvious pulmonary edema, limitation of intravenous fluid administration unless fluid loss is excessive, and avoidance of hyperosmotic agents
  4. Delivery of the fetus to achieve a remission of preeclampsia.

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Which patients should be given Magnesium Sulfate?

- the 2013 Task Force recommends that women with either eclampsia or severe preeclampsia should be given magnesium sulfate neuroprophylaxis.
- At the same time, however, the 2013 Task Force suggests that all women with "mild" preeclampsia do not need magnesium sulfate neuroprophylaxis.

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Which patients should be given Magnesium Sulfate?

TABLE 40-15. Selective versus Universal Magnesium Sulfate Prophylaxis: Parkland Hospital Criteria to Define Severity of Gestational Hypertension

In a woman with new-onset proteinuric hypertension, at least one of the following criteria is required:

Systolic BP ≥ 160 or diastolic BP ≥ 110 mm Hg
Proteinuria ≥ 2+ by dipstick in a catheterized urine specimen
Serum creatinine > 1.2 mg/dL
Platelet count < 100,000/μL
Aspartate aminotransferase (AST) elevated two times above upper limit of normal range
Persistent headache or scotomata
Persistent midepigastric or right-upper quadrant pain

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 24th edition; 2014; chap 40 Hypertensive disorders

Management of Eclampsia

Magnesium Sulfate to Control Convulsions

- magnesium sulfate administered parenterally is an effective anticonvulsant that avoids producing central nervous system depression in either the mother or the infant. It may be given intravenously by continuous infusion or intramuscularly by intermittent injection
- Because labor and delivery is a more likely time for convulsions to develop, women with preeclampsia-eclampsia usually are given magnesium sulfate during labor and for 24 hours postpartum.
- Magnesium sulfate is not given to treat hypertension.

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018 chap 40 Hypertensive disorders

TABLE 40-11. Magnesium Sulfate Dosage Schedule for Severe Preeclampsia and Eclampsia

Continuous Intravenous (IV) Infusion

Give 4- to 6-g loading dose of magnesium sulfate diluted in 100 mL of IV fluid administered over 15–20 min
Begin 2 g/hr in 100 mL of IV maintenance infusion. Some recommend 1 g/hr
Monitor for magnesium toxicity:
- Assess deep tendon reflexes periodically
- Some measure serum magnesium level at 4–6 hr and adjust infusion to maintain levels between 4 and 7 mEq/L (4.8 to 8.4 mg/dL)
- Measure serum magnesium levels if serum creatinine ≥ 1.0 mg/dL

Magnesium sulfate is discontinued 24 hr after delivery

Intermittent Intramuscular Injections

Give 4 g of magnesium sulfate ($MgSO_4 \cdot 7H_2O$ USP) as a 20% solution intravenously at a rate not to exceed 1 g/min
Follow promptly with 10 g of 50% magnesium sulfate solution, one half (5 g) injected deeply in the upper outer quadrant of each buttock through a 3-inch-long 20-gauge needle. (Addition of 1.0 mL of 2% lidocaine minimizes discomfort.) If convulsions persist after 15 min, give up to 2 g more intravenously as a 20% solution at a rate not to exceed 1 g/min. If the woman is large, up to 4 g may be given slowly
Every 4 hr thereafter, give 5 g of a 50% solution of magnesium sulfate injected deeply in the upper outer quadrant of alternate buttocks, but only after ensuring that:
- The patellar reflex is present,
- Respirations are not depressed, and
- Urine output the previous 4 hr exceeded 100 mL

Magnesium sulfate is discontinued 24 hr after delivery

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 24th edition; 2014; chap 40 Hypertensive disorders

Management of Eclampsia

Magnesium Sulfate toxicity

- Eclamptic convulsions are almost always prevented or arrested by plasma magnesium levels maintained at **4 to 7 mEq/L** (4.8 to 8.4 mg/dL, or 2.0 to 3.5 mmol/L)
- Patellar reflexes disappear when the plasma magnesium level reaches 10 mEq/L—about 12 mg/dL—presumably because of a curariform action. This sign serves to warn of impending magnesium toxicity.

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Management of Eclampsia

Magnesium Sulfate toxicity

- When plasma levels rise above 10 mEq/L, breathing becomes weakened.
- At 12 mEq/L or higher levels, respiratory paralysis and respiratory arrest follow.
- Treatment with **calcium gluconate or calcium chloride**, 1 g intravenously, along with withholding further magnesium sulfate, usually reverses mild to moderate respiratory depression.

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Principles of Management of Eclamptic Seizures

Maintain situational awareness. An eclamptic seizure is dramatic and disturbing. The attending clinician is challenged to maintain a purposeful calm and to avoid unnecessary interventions that can result in iatrogenic complications.[33]

Avoid polypharmacy. Do not attempt to shorten or abolish the initial convulsion by using drugs such as diazepam (Valium) or phenytoin (Dilantin). Magnesium sulfate is the drug of choice for initial and recurrent convulsions. Polypharmacy can lead to maternal or neonatal respiratory depression, aspiration, or other adverse effects.

Protect the airway, and minimize the risk of aspiration. Place the patient on her left side and suction her mouth. Call for someone skilled in intubation to be immediately available.

Prevent maternal injury. Falls from the bed can result in contusions or fractures, and head injury may result from violent seizure activity. Close observation and use of soft padding and side rails on the bed may help prevent injuries.

Administer magnesium sulfate to control convulsions. If the patient has already received a prophylactic loading dose and is receiving a continuous infusion when the seizure occurs, an additional 2 g should be given intravenously. Otherwise, a 4- to 6-g loading dose should be given intravenously over 15 to 20 minutes, followed by a continuous infusion of 2 g per hour. The loading dose and subsequent bolus should not total more than 8 g for a recurrent seizure.[33]

Follow delivery plan. Avoid the temptation to perform immediate cesarean delivery for a self-limited seizure episode.

Leeman et al. Am Fam Physician. 2016 Jan 15;93(2):121-127

Serious complications of severe hypertension

1. placental abruption
2. HELLP syndrome
3. pulmonary edema
4. renal failure
5. eclampsia
6. Perinatal/maternal death
7. Hypertensive encephalopathy
8. Ruptured liver hematoma

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Management of Severe Hypertension

- National High Blood Pressure Education Program Working Group (2000) and the 2013 Task Force recommend treatment to lower systolic pressures to or below 160 mm Hg and diastolic pressures to or below 110 mm Hg.
- Long-standing hypertension results in development of **Charcot-Bouchard aneurysms** in the deep penetrating arteries of the lenticulostriate branch of the middle cerebral arteries.

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Antihypertensive agents

1. **Hydralazine IV**

- administered IV with a 5-mg initial dose, followed by 5- to 10-mg doses at 15- to 20-minute intervals until a satisfactory response is achieved
- limit the total dose to 30 mg per treatment cycle
- target response antepartum or intrapartum is a decrease in diastolic blood pressure to 90 to 110 mm Hg.
- Lower diastolic pressures risk compromised placental perfusion.

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Antihypertensive agents

2. Labetalol

- Alpha 1- and nonselective β-blocker.
- Some prefer its use over hydralazine because of fewer side effects
- the American College of Obstetricians and Gynecologists (2012b) recommends starting with a 20-mg intravenous bolus. If not effective within 10 minutes, this is followed by 40 mg, then 80 mg every 10 minutes. Administration should not exceed a 220-mg total dose per treatment cycle.

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Antihypertensive agents

3. Nifedipine

- calcium-channel blocking agent has become popular because of its efficacy for control of acute pregnancy-related hypertension.
- Royal College of Obstetricians and Gynaecologists (2006) recommend a *10-mg initial oral dose to be repeated in 30 minutes if necessary.*
- Nifedipine given sublingually is no longer recommended.

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018 chap 40 Hypertensive disorders

Antihypertensive agents

4. Diuretics

- Potent loop diuretics can further compromise placental perfusion.
- Immediate effects include depletion of intravascular volume, which most often is already reduced compared with that of normal pregnancy
- *before delivery, diuretics are not used to lower blood pressure*
- We limit antepartum use of furosemide or similar drugs solely to treatment of pulmonary edema

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Antihypertensive agents

5. Other Antihypertensive Agents

- A few other generally available antihypertensive agents are not widely used:
  1. *verapamil (Ca channel antagonist) by intravenous infusion at 5 to 10 mg per hour.*
  2. *nimodipine given either by continuous infusion or orally*
  3. *intravenous ketanserin, a selective serotonergic (5HT2A) receptor blocker.*
  4. *Nitroprusside or nitroglycerine is recommended by some if there is not optimal response to first-line agents → fetal cyanide toxicity may develop after 4 hours.*

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

Dosing of Hydralazine, Labetalol, and Nifedipine for Severe Preeclampsia

Hydralazine, 5 to 10 mg IV over 2 minutes. If systolic BP ≥ 160 mm Hg or diastolic BP ≥ 110 mm Hg after 20 minutes, administer an additional 10 mg IV. If above threshold BP after an additional 20 minutes, switch to IV labetalol.[A1] May use constant IV infusion at rate of 0.5 to 10 mg per hour.[A2]

Labetalol, 20 mg IV initial dose. If the initial dose is not effective, double to 40 mg and then again to 80 mg at 10-minute intervals until target BP is reached. If systolic BP ≥ 160 mm Hg or diastolic BP ≥ 110 mm Hg after the 80-mg dose, switch to IV hydralazine.[A3,A4] The maximal dosage of IV labetalol is 220 to 300 mg in 24 hours.[A1,A3]

Nifedipine, 10 mg oral initial dose. If systolic BP ≥ 160 mm Hg or diastolic BP ≥ 110 mm Hg after 30 minutes, administer an additional 20 mg orally. If above threshold BP 30 minutes after second dose, administer additional 20 mg. May then administer 10 to 20 mg every 4 to 6 hours.[A1]

Leeman et al. Am Fam Physician. 2016 Jan 15;93(2):121-127

Fluid Therapy

- Lactated Ringer solution is administered routinely at the rate of 60 mL to no more than 125 mL per hour unless there is unusual fluid loss from vomiting, diarrhea, or diaphoresis, or, more likely, excessive blood loss with delivery.
- Do not be tempted to increase IV fluids vigorously due to oliguria.
  - *A controlled, conservative fluid administration is preferred for severe preeclampsia who already has excessive extracellular fluid that is inappropriately distributed between intravascular and extravascular spaces.*
  - *infusion of large fluid volumes enhances the maldistribution of extravascular fluid and thereby appreciably increases the risk of pulmonary and cerebral edema*

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 25th edition; 2018; chap 40 Hypertensive disorders

SUMMARY

- 4 Types of hypertensive disorders in pregnancy
- Diagnosis
- Risk factors
- Etiopathogenesis
- Prevention
- Treatment

Thank you!

youtube channel: Ina Irabon

www.wordpress.com: Doc Ina OB Gyne