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Video Case

Pre-eclampsia, Eclampsia & Gestational Hypertension

Objectives:

- → Classify hypertensive disorders of pregnancy
- → Describe the pathophysiology of preeclampsia-eclampsia
- → List risk factors for preeclampsia
- → Recognize the signs and symptoms to diagnose preeclampsia-eclampsia
- → Explain the management of a patient with preeclampsia-eclampsia
- → List the maternal and fetal complications associated with preeclampsia-eclampsia

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Female presentation

Video Case | Editing File

1. Preeclampsia

Definition:

- Preeclampsia is **NEW ONSET** of sustained **elevation of BP ≥140/90** mmHg **after 20 weeks'** gestation **with** proteinuria in the **absence of preexisting hypertension**,
- When preeclampsia arises in the **early second trimester (14 to 20 weeks)**, a **hydatidiform mole** or **choriocarcinoma** should be considered .
- **It is a known risk associated with high risk pregnancy.**

Types :

1. Preeclampsia **without** severe features

2. Preeclampsia **with** severe features

Pathophysiology:

During pregnancy fetal drive cytotrophoblast invade the maternal uterine spiral arteries and replace their endothelium converting the high resistance small diameter vessels into high capacitance low resistance vessels to ensure adequate delivery of maternal blood to the placenta as you can see in this healthy placenta the spiral artery is lined with cytotrophoblast making it nice and wide to ensure a lot of blood flow.

- In a woman destined to develop preeclampsia later in her pregnancy this process not occur correctly and the arteries remain narrow decreasing blood flow to the placenta and causing hypoxemia.

Studies have shown abnormalities in vasculargenic and angiogenic signaling pathways with the exact mechanism for this abnormal trophoblast invasion remains unclear

- The pathophysiology of preeclampsia with severe features is the same as preeclampsia, but involves severe diffuse vasospasm and more intense capillary injury to where the ischemia demonstrates itself in overt, usually multiorgan system injury .

Risk factors:

- **History of preeclampsia** in previous pregnancies (the biggest risk factor)
- Preeclampsia in a first degree relative.
- Age extremes (>40).
- obesity.
- Primiparas : a woman who is giving birth for the first time
- Multiple gestation.
- Maternal past medical history (Hypertension , Renal disease , DM , Hypercoagulability ,SLE).
- Hydatidiform mole.

OB Triad :

Preeclampsia

- Pregnancy >20 wk
- Sustained HTN (>140/90 mm Hg)
- Proteinuria (≥300 mg/24 h)

it is important to note that most cases of preeclampsia occur and healthy nulliparous woman with no other obvious risks

1. Preeclampsia

Diagnosis:

- **Sustained BP elevation** of ≥140/90 mmHg on 2 occasions at least 4 hours apart after 20 weeks gestation **and one of the following :**

1. **Proteinuria** :
   - ≥300 mg on a 24 h urine collection (The most accurate way)
   - protein/creatinine ratio of ≥0.3
   - Urine dipstick (protein > 1+) Usually we use it as a first step to diagnose proteinuria & considered a screening test.
2. **OR Systematic finding** " +/- proteinuria " , it is a **preeclampsia <u>with</u> severe features** (One feature from the criteria is enough) :
   - Elevated liver enzyme at least twice normal Concentration
   - Thrombocytopenia (the most common abnormality)
   - Serum creatinine > 1.1
   - Pulmonary edema
   - New onset cerebral or **visual symptoms** Due to constricted vessels.

BOX 14-1

CRITERIA FOR SEVERE PREECLAMPSIA

- Severe hypertension (systolic BP ≥160 mm Hg or diastolic BP ≥110 mm Hg) at rest on two occasions at least 4 hr apart*
- Renal insufficiency (serum Cr >1.1 mg/dL or doubling of baseline values)
- Cerebral or visual disturbances
- Pulmonary edema
- Epigastric or right upper quadrant pain
- Elevated liver enzymes (AST or ALT at least two times normal level)
- Thrombocytopenia (platelet count <100,000/μL)

Based on the American College of Obstetricians and Gynecologists Executive Summary: Hypertension in pregnancy, 2013.
ALT, Serum alanine aminotransferase; *AST,* serum aspartate aminotransferase; *BP,* blood pressure; *Cr,* creatinine.
*4-hr delay not required if antihypertensive therapy is initiated.

In **preeclampsia** the symptoms and physical findings (if present) are generally related to :
Excess weight gain (gaining 5 pounds = 2.5 kg in 1 week is pathological not physiological) & fluid retention & edema (eneralized edema " especially hand and face")

To make it easy , Pre eclampsia is new onset of : elevated BP + proteinuria
Then look for other symptoms ,

- Don't have ? it is **preeclampsia <u>without</u> severe features**
- Have any symptoms from severe preeclampsia criteria (not necessary to have proteinuria) ? it is **preeclampsia <u>with</u> severe features**

Complications :

Complications can include progression from preeclampsia without severe features to preeclampsia with severe features .

Maternal complications:

- **Eclampsia** : may occur before, during or after labor and result in high perinatal and maternal morbidity and mortality (the goal is always to prevent eclampsia).
- **HELLP Syndrome**
- Stroke
- Liver injury subcapsular hematoma & hepatic rapture
- Kidney injury renal failure - acute tubular necrosis "dark urine"
- Acute respiratory distress syndrome / ARDS
- Maternal Death : Preeclampsia/eclampsia is one of the leading causes of maternal mortality in United state . The mortality is primarily **due to central nervous system (CNS) hemorrhage.**

Fetal complications:

- Placental abruption
- Fetal growth restriction
- Preterm delivery
- Fetal death

1. Preeclampsia

Management:

The only definitive cure is delivery and removal of all fetal-placental tissue.

- The mode of delivery should be decided by :
  - Fetal presentation
  - Cervical status fetal
  - Gestational age
  - Maternal fetal condition

- The management of patient with preeclampsia involves:
  - The rest of maturity of the fetus
  - The rest of maternal morbidity of worsening disease progression

Preeclampsia <u>without</u> severe features :

- A woman with preeclampsia without evidence of fetal compromise or appear to be severe or progressing managed by **close surveillance until 37 weeks** estimated gestational age, this involves:
  - Monitoring the mother carefully with :
    - Frequent blood pressure monitoring
    - Serum and urine evaluation to watch for disease progression
  - Monitoring the fetus with :
    - Ultrasound for fetal growth , if evidence of restriction is found ?
      - Fetal placental assessment including Umbilical artery Doppler velocimetry is recommended.
    - The fetus should be monitored with twice weekly non-stress test
    - Betamethasone should be administered for fetal lung maturity prior to 34 weeks estimated gestational age.
- It will generally not be delivered unless the gestational age is **37 weeks or older** to minimize neonatal complications of prematurity.

Preeclampsia <u>with</u> severe features :

- **More than 34 week**s' gestation : **delivery** after a brief period of stabilization.
- **Less than 34 weeks**' gestation : initial stabilization of the patient :
  - Magnesium sulfate for seizure prophylaxis
  - + Corticosteroids for fetal lung maturity
  - + Medical control of severe hypertension
- Then monitoring :
  - **Stable** and r**each to 34 weeks** ? **Delivery**
  - Still **Unstable** / **Evidence of HELLP syndrome or Eclampsia** / There is **deterioration in clinical status** (e.g., uncontrollable hypertension, deteriorating renal or liver function, pulmonary edema, coagulopathy, CNS symptoms, abruption, or abnormal fetal testing) ? **Delivery**

1a. Eclampsia

Definition:

Eclampsia is the presence of **unexplained generalized seizures** (grand mal seizures) in a hypertensive, proteinuric pregnant woman in the last half of pregnancy .

Pathophysiology:

Severe diffuse cerebral vasospasm resulting in cerebral perfusion deficits and cerebral edema .

Risk Factors:

- Are the same as in preeclampsia .
- A primary seizure disorder does not predispose to eclampsia .

Management:

- Eclampsia is a true obstetric **emergency**.
- It is critically important to stabilize the mom first for this will stabilize the fetus.
  1. **Protect the mother 's airway and tongue**
  2. **Give oxygen** by face mask to relieve hypoxia .
  3. **Administer MgSO4** (the initial step and drug of choice for management) with an IV bolus of 5 g **to stop seizures**, continuing maintenance infusion rate of 2 g/h. Continue IV MgSO4 for 24 hours after delivery. but if no IV access we give it IM. (**Possible MCQs**)
     - When you give Magnesium sulfate (MgSO4) , you should assess the patient's deep tendon reflexes, because if the patient lose (decrease) deep tendon reflexes while on Magnesium, it is a sign that if Magnesium is continued, it will decrease her respiratory drive, cut off diaphragm and have her not breath.
     - **Possible MCQ: first sign of MgSO4 toxicity is ?** loss of patellar reflex.
       - **Magnesium sulfate toxicity ?** → give calcium gluconate as antidote.
  4. **Lower diastolic BP** between 90–100 mm Hg with IV hydralazine and/or labetalol (blood pressure and pulse oximetry should be recorded every 10 minutes with the patient in the lateral position)

Aggressive prompt delivery is indicated for **eclampsia at any gestational age after stabilization of the mother and the fetus**.
Attempt vaginal delivery with IV oxytocin infusion if mother and fetus are stable, If not do C-section .

Eclamptic seizures often induce a fetal bradycardia that usually resolves after : maternal stabilization and correction of hypoxia .

TABLE 14-2
CLINICAL CORRELATES OF SERUM MAGNESIUM SULFATE LEVELS

Clinical Response	Serum Levels* (mg/dL)
Loss of patellar reflex	8-12
Warmth and flushing	9-12
Somnolence	10-12
Slurred speech	10-12
Paralysis and respiratory difficulty	15-17
Cardiac arrest	30-35

*Therapeutic range: 4.8-9.6 mg/dL.

Complications:

- Intracerebral hemorrhage.
- Possible death.

1b. HELLP Syndrome

Definition:

HELLP syndrome occurs in 5–10% of preeclamptic patients and it's a sign of severe preeclampsia
It is characterized by :

- Hemolysis **(H), Which blood tests show hemolysis?**
  - Schistocyte in the peripheral blood smear
  - Increase LDH
  - Increase bilirubin
  - Decrease haptoglobin
  - Decrease hemoglobin
- **Elevated liver enzymes (EL)** (ALT/AST) , What if the ALP is high, do we order it in pregnancy? No, it's normally elevated in pregnancy because it's produced by placenta as well.
- **Low platelets (LP)** (Normal count 150,000-450,000)
- Elevated creatinine and serum uric acid because the excretion is decrease from the kidney.

Differential Diagnosis: It can be confused with thrombotic thrombocytopenic purpura and hemolytic uremic syndrome. HTN, although frequently seen, is not always present .

Risk Factors:

HELLP syndrome occurs two times as often in multigravidas as primigravidas .

Management:

- Prompt delivery is indicated for **HELLP SYNDROME** **at any gestational age** after stabilization of the mother and the fetus.
- Use of maternal **corticosteroids** may enhance postpartum normalization of liver enzymes and platelet count .

Complications:

Complicating conditions associated with HELLP include :

- DIC.
- Abruptio placentae.
- Fetal demise.
- Ascites.
- Hepatic rupture.

OB Triad :

HELLP Syndrome
- Hemolysis
- ↑ liver enzymes
- ↓ platelets

2. Gestational Hypertension

Definition:

- Gestational hypertension is diagnosed with **NEW ONSET** of sustained **elevation of BP ≥140/90** mmHg **after 20 weeks** of pregnancy or **within 48 to 72 hours** of delivery **without** proteinuria or any symptomatic finding of preeclampsia.
- Physical findings are unremarkable for pregnancy .
- Laboratory tests are unremarkable for pregnancy**.** End organ damage is absent as well.

Diagnosis:

- Is made with sustained elevation of BP >140/90 mm Hg **without proteinuria** (key finding) .
- The diagnosis of gestational hypertension can only be made in retrospect, if the pregnancy has been completed without :
  - The development of proteinuria or other evidence of preeclampsia,
  - AND if the blood pressure has returned to normal before the 12th week postpartum.

Management:

- Conservative outpatient management with close observation since 30% of patients will develop preeclampsia.
- More frequent assessments and follow ups and Appropriate lab testing should be performed to rule out preeclampsia, e.g., urine protein, hemoconcentration assessment .
- US assessing for intrauterine growth restriction.
- Deliver at 37 weeks .

OB Triad :

Gestational Hypertension
- Pregnancy >20 wk
- Sustained HTN (≥140/90 mmHg)
- No proteinuria

TAKE A BREAK

3+4. Chronic Hypertension and Superimposed Preeclampsia

Definition:

- **Chronic HTN** is made when BP ≥140/90 mm Hg with onset before the pregnancy or before 20 weeks' gestation.
    - **Superimposed preeclampsia** involves signs and symptoms of preeclampsia along with chronic hypertension after the 20th week of pregnancy.

Diagnosis:

Chronic HTN :

- **BP ≥140/90 mmHg with onset before the pregnancy or before 20 weeks' gestation .**
    - Without any sign of preeclampsia : **present or worsening of proteinuria** (worsening in pt with nephropathy) **- thrombocytopenia - elevated Liver Enzymes ....**

Superimposed preeclampsia :

- **chronic HTN along with :**
    - Develop sudden significant increases in blood pressure, present "if pt didn't have nephropathy" or worsening of proteinuria, or any of the other signs and symptoms of preeclampsia.

Management:

- **Chronic HTN :**
  Conservative outpatient management for uncomplicated mild-to-moderate **chronic HTN** .
    - **Stop drug therapy:** Attempt discontinuation of antihypertensive agents that are potentially teratogenic, Follow guideline outlined.
        - Fortunately, many women, blood pressures will decrease to normal in the second trimester, and no antihypertensive medication will be needed.
    - Give aspirin
    - **Serial BP and urine protein** assessment is indicated for early identification of superimposed preeclampsia .
    - **Serial sonograms and antenatal testing** are appropriate after 30 weeks' gestation to monitor for increased risk of IUGR .
    - **Induce labor at 37- 38 - 39+6 weeks** .

- **Superimposed preeclampsia :**
  According to UP TO DATE : upon diagnosis of superimposed preeclampsia, management of patient with chronic hypertension is generally similar to that of other patients with preeclampsia.

3+4. Chronic Hypertension and Superimposed Preeclampsia

Complications:

Complications can include progression from chronic HTN to superimposed preeclampsia, which can lead to maternal and fetal death .

Maternal complication:

- HELLP Syndrome.
- CNS: eclamptic seizure, stoke.
- Hepatic: subcapsular hematoma.
- Renal: acute tubular necrosis "dark Black urine".
- Hematological: hemorrhage, DIC.

Fetal complication:

- Preterm delivery
- **Placental abruption** due to high blood pressure
- Fetal growth restriction
- Fetal death.

OB Triad :

Chronic HTN:
- Pregnancy <20 wk or pre pregnancy
- Sustained HTN (>140/90 mm Hg)
- +/– proteinuria

OB Triad :

Superimposed Preeclampsia:
- Chronic HTN
- Worsening BP or proteinuria or sign of preeclampsia

Antihypertensive Drug Therapy Issues:

- The American College of Obstetricians and Gynecologists recommend antihypertensive therapy for women with:
  - Chronic hypertension at a systolic BP≥160 mmHg or diastolic BP≥110 mmHg
  - Preeclampsia and a sustained systolic BP≥160 mmHg and/or diastolic BP≥110 mmHg
    - **The goal of antihypertensive therapy in severe preeclampsia is to stabilize the mother by lowering blood pressure carefully to prevent CNS hemorrhage (Maternal CVA)**
- **The drug of choice for hypertensive pregnant women is methyldopa** because of extensive experience and documented fetal safety or **labetalol** and **hydralazine** (The safest, most efficacious drugs for the acute control of severe hypertension complicating preeclampsia) or **calcium channel blockers (ex.nifedipine).**
  - We don't give nifedipine with magnesium sulphate if we use nifedipine as a tocolytic agent.
- **"Never use" medications :**
  - **Angiotensin-converting enzyme inhibitors** are contraindicated in pregnancy, as they have been associated with fetal hypocalvaria, renal failure, oligohydramnios, IUGR and death.
  - **Angiotensin II receptor blockers, renin inhibitors, and mineralocorticoid blockers** should be avoided at all stages of pregnancy because of potential fetal toxicity.
  - **Diuretics** should not be initiated during pregnancy owing to possible adverse fetal effects of associated plasma volume reduction unless there is evidence of pulmonary edema.
- **BP target range :** 120-160/80-110 mmHg according to American Heart Association.
- **Discontinuing medications** Pharmacologic treatment in patients with diastolic BP <90 mm Hg or systolic BP <140 mm Hg does not improve either maternal or fetal outcome.

Teaching case

An 18 year old **G1P0** currently at **38** 0/7 weeks presents for her routine prenatal visit. She has had an uncomplicated pregnancy up to this point, with the exception of a late onset of prenatal care and obesity (BMI of 35 kg/m^2). She reports that during the past week, she has noted some **swelling of her hands and feet.** She also has been feeling a bit more **fatigued** and has had a **headache on and off.** She reports good fetal movement. She has had some contractions on and off, but nothing persistent. Her blood pressure is **147/92** and her urine dip has **1+ protein**/no ketones/no glucose. The fundal height measures 36 cm, the fetus is cephalic with a heart rate of 144 bpm. On physical exam you note that the patient has **3+ pretibial edema**, and **trace edema of her hands and face**. She has 2+ deep tendon reflexes and 2 beats of clonus. You review her blood pressures up to this point and note that at the time of her first prenatal visit at 18 weeks, her blood pressure was 130/76 and she had no protein in her urine. However, since that visit, her blood pressures seem to have been climbing higher with each visit. Her last visit was one week ago, and she had a blood pressure of 138/88 with trace protein in the urine and she has gained 5 pounds

Q1 What is considered a hypertensive blood pressure during pregnancy ?

In pregnancy, hypertension is defined as either a systolic blood pressure ≥ 140 or diastolic blood pressure ≥ 90 or both .

Q2 What types of hypertensive syndromes can occur during pregnancy ?

- **Chronic hypertension :** Requires that the patient have documented hypertension preceding 20 weeks gestation, or prior to conception, or where hypertension is first noted during pregnancy and persists for longer than 12 weeks postpartum .
- **Preeclampsia-eclampsia :** Development of new onset **hypertension** and **proteinuria** or any systemic findings **after 20 weeks** of pregnancy. Is stratified into mild and severe forms. There are atypical forms of preeclampsia as well(for example HELLP syndrome).
- **Preeclampsia superimposed on chronic hypertension :** Superimposed preeclampsia should be reserved for those women with chronic hypertension who develop new-onset proteinuria (≥ 300 mg in a 24-hour collection) after the 20th week of pregnancy. In pregnant women with pre existing hypertension and proteinuria, the diagnosis of superimposed preeclampsia should be considered if the patient experiences sudden significant increases in blood pressure or proteinuria or any of the other signs and symptoms consistent with severe preeclampsia. (Preeclampsia comes after chronic hypertension)
- **Gestational Hypertension :** Hypertension without proteinuria or clinical manifestations which first appears after 20 weeks gestation or within 48 to 72 hours after delivery and resolves by 12 weeks postpartum .

Teaching case

Q3 How does the physiology of preeclampsia lead to the clinical symptoms and findings ?

- Hypoxia, hypoperfusion and ischemia lead to the clinical placental pathophysiology (with fetal compromise: IUGR, oligohydramnios, placental abruption) .
- Systemic endothelial dysfunction leads to central & peripheral edema, proteinuria, and hypertension (from disruption of vascular regulation). Endothelial dysfunction in target organs leads to headache, epigastric pain, and renal dysfunction.
- Microvascular endothelial destruction leads to release of procoagulants and DIC .

Q4 What are the laboratory findings that support a diagnosis of preeclampsia-eclampsia syndrome ?

- Proteinuria (> 300 mg on a 24 hour urine collection) or increased urine protein/creatinine ratio > 0.3
- Increased serum creatinine (normally in pregnancy is low)(Cr>1.1 mg/dL or doubling the baseline values)
- Hemolysis Decreased Hb - decreased haptoglobin - increased LDH - increased Bilirubin - increased reticulocyte
- Thrombocytopenia (< 100,000 cells/mm3)
- Elevated hematocrit
- Elevated liver enzymes (ALT/AST twice normal)
- Elevated serum uric acid concentration (it's not a feature)
- Coagulation profile (DIC)

The diagnosis of this case is ?

Mild Preeclampsia.

What's the management is this case?

Delivery

Risk factors to develop preeclampsia in this case?

- Obesity
- Primigravida

Teaching case

Q5 What types of maternal and fetal complications are associated with preeclampsia-eclampsia syndrome ?

- **Maternal :**
  - **CNS :** eclamptic seizure, stroke We give magnesium sulfate as a first line to avoid seizure
  - **Cardiopulmonary :** pulmonary edema
  - **Hepatic :** Subcapsular hematoma or hepatic rupture
  - **Renal :** renal failure or acute tubular necrosis Severe right upper quadrant pain
  - **Hematologic :** hemorrhage, DIC
  - Maternal death (especially eclampsia)

- **Fetal :**
  - Preterm delivery Because of preeclampsia that starts very early
  - Placental abruption Due to elevated B.P
  - Fetal growth restriction (The most common cause of Fetal growth restriction is incorrect date- there is two types early and late- the late Fetal growth restriction most commonly caused by uteroplacental insufficiency)
  - Hypoxic ischemic encephalopathy
  - Fetal death
  - Oligohydramnios why? Because the blood supply to the placenta decreased-The nutrients decrease (the blood will shift to the three major vital organs of the baby which is the brain, heart and adrenals-as a result the blood flow to the renal system becomes low and GFR decreases which leads to oligohydramnios)

Dr's notes 441

- **Standardized maternal tests:** CBC, LDH, coagulation profile, renal study, 24 hrs protein urine and liver function test.

- **The most common obstetric causes of maternal mortality worldwide?**
  Haemorrhage, Preeclampsia, Sepsis

- **The most common non-obstetric (medical)causes of maternal mortality?**
  Cardiovascular disease,PE or Thrombophilia ,HTN and DM with complications.

- **Always remember!**
  - Some women have essential hypertension before pregnancy.
  - Some women get diagnosed with chronic hypertension during pregnancy before 20 weeks of gestation.
  - After 20 weeks of gestation you have to be careful, is it associated with proteinuria or end organ damage or is it just elevated blood pressure? Cause the management of each types is different!

- **What are types of hypertensive disorders of pregnancy?**
  - Preeclampsia
    - Eclampsia and HELLP syndrome are complication **not** a type
  - Gestational HTN
  - Chronic HTN
  - Chronic HTN with superimposed preeclampsia

- History: eclampsia: in Greek means lighting referred to sudden symptoms / Preeclampsia: toxemia of pregnancy, a term that originated in the mistaken belief that the condition was caused by toxins.

- In the questions they will give a scenario and ask which type of hypertensive disorders of pregnancy this case.The definition of each type is important.
  - **How to differentiate?**
    By Timing, ex : Preeclampsia after 20 weeks of gestation.

- **Why Preeclampsia happens after 20 weeks of gestation?**
  Because of abnormal development of placenta (at 16-20 weeks of gestation abnormality happens).
  - The pathophysiology (not fully understood) :
    - Embryology Blastocysts divided into two parts:
      - Inner mass develop to an embryo
      - Outer layer trophoblast gives placenta (The problem within the cytotrophoblast)
    - Abnormal vasoconstriction occur in the decidua due to abnormal invasion
    - Secrets in the maternal circulation some substances 6-Low placental growth factor and elevated tyrosine kinase

- Due to this pathogenesis, we give a low dose of **aspirin** to prevent the recurrence in the next pregnancy between 12-16 weeks of gestation , it work by reduces Thromboxane A2 and increases prostacyclin.

- The risk of recurrence of preeclampsia in the next pregnancy is 20%.

Dr's notes 441

- Important component of preeclampsia is HTN + Proteinuria (300mg/24h urine collection is significant)

- Definition of HTN have been changed in the guidelines now => 135/85 (130/80 in medicine HTN lecture) but in the pregnancy still the same => 140/90 (2 reading in 4h apart).

- We can use a urine dipstick but we need 2 dipsticks to confirm (+1 or more) but it is the lowest sensitive test for proteinuria.
    - Sometimes when there's vaginal discharge you might get 1+ proteinuria and it's just a contaminated sample.

- **Why do we have proteinuria with preeclampsia?**
  In normal pregnancy GFR increases 50%, Sometimes with preeclampsia it can decrease GFR and decrease in renal blood flow results from constriction of the afferent arteriolar system. This afferent vasoconstriction may eventually lead to damage to the glomerular membranes, thereby increasing the permeability of these membranes to proteins

- Edema was one of the criteria to diagnose preeclampsia now they removed it because 50% to 80% of all pregnant women have edema so it is not a hallmark for preeclampsia.

- Preeclampsia I think it's the only disease in obstetric and gynecology its risk factor is nulliparity.

- **What is the absolute treatment of preeclampsia?**
  Delivery. get out of the source which is placenta.

- **Why HELLP syndrome happens?**
  There is endothelial injury.

- 20% of patients with HELLP syndrome don't have high blood pressure and 16% don't have proteinuria. Diagnosis made by exclusion in this case.but the most common in HELLP syndrome they present with HTN and proteinuria.

- **Patient with severe blood pressure 165/113 with proteinuria and thrombocytopenia?**
  This is severe preeclampsia /not HELLP syndrome you should have the triad to diagnose HELLP syndrome.

- **If the patient with severe preeclampsia and you failed to stabilize her (deteriorating) and she's 32 weeks** ?
  Deliver her you can't wait.

- **If the patient has severe preeclampsia but she is stable now and she's 32 weeks for example?**
  we can wait to deliver her after 34 weeks of gestation.

- **if the patient has mild preeclampsia and i can stabilize the patient ?**
  Deliver at 37 weeks of gestation.

Dr's notes 441

- **Patient with severe preeclampsia in 32 weeks ?**
  give magnesium sulphate and steroids because if she's deteriorating we can deliver her as soon as possible.

- **First sign of magnesium sulphate toxicity is ?**
  loss of patellar reflex then respiratory depression then cardiac toxicity and arrest , Due to the toxicity we check the magnesium level and patellar reflex .

- We do auscultation because they can develop pulmonary edema from preeclampsia and it could be also due to magnesium sulphate toxicity.

- **What is the only absolute contraindication of magnesium sulphate?**
  Myasthenia gravis.
  - **The alternative for magnesium sulphate in patients with myasthenia gravis is ?**
    phenytoin.

- **The antidote in case of magnesium sulphate toxicity is ?**
  calcium gluconate 1 gm.

- **What are the obstetric uses for magnesium sulphate?**
  - Prevention of eclampsia in patients who have preeclampsia with severe features
  - Treatment of eclampsia.
  - Neuroprotection "decreases the rate of cerebral palsy" For the fetus from 24-before 32 weeks of gestation

  (uses of $MgSO_4$ up to 32 for fetal protection, and more than 32 week when mother need it " maternal benefit ").

- **The only two medications that can cross to the baby with good therapeutic concentrations are ?**
  betamethasone and dexamethasone.

- **For fetal lung maturation there are two medications ?**
  Betamethasone and Dexamethasone.

- **Why not give oral corticosteroids?**
  Because placenta has enzymes protecting the baby.

- Betamethasone (2 doses /24 h and dexamethasone 4 doses / 12 h) the duration is 48 h.

- **The advantage of steroids to the fetus ?**
  1-Decrease the respiratory distress syndrome
  2- Decrease necrotizing enterocolitis
  3- Decrease intraventricular haemorrhage

- Steroids given from 24-less than 34 weeks of gestation.

Dr’s notes 441

- Preeclampsia is supposed to be improving after delivery so we will continue postpartum the anti-hypertensive medication that she is taking during pregnancy and reduce the dose until she goes back to normal then stop the medication.

- If the patient has chronic HTN postpartum she will go back again to the anti-hypertensive medication that she takes before the pregnancy.

- We don’t give methyldopa postpartum because it increases the risk of postpartum depression, instead we use nifedipine or labetalol.

- **How to confirm it’s gestational HTN?**
  If it resolves after 12 weeks and no proteinuria

- Chronic HTN persists beyond 12 weeks postpartum.

Summary (Hacker's & Moore's)

Done by the AMAZING Hessa Fahad ❤️

Initial evaluation of preeclampsia

Hx	**Look for:** • **Sever features?** (headache, visual changes, n/v, abdominal or epigastric pain, and vaginal bleeding.) • **Evidence of fetal compromise** (IUGR, oligohydramnios or FHR abnormalities) • **EGA ?** (is the fetus mature enough for a reasonably uncomplicated course after delivery?) because delivery is the only definitive cure of preeclampsia • **PMH** (during, before pregnancy): high BP, renal disease ?
PE	• BP • Weight gain • Edema • Fundal height • Epigastric or RUQ tenderness • Uterine tenderness • Sign of pulmonary edema • Reflexes (hyperreflexia indicate vulnerability to seizures) • Ophthalmic examination (only if there are visual symptoms or headache)
Fetal Evaluation	1. Accurate determination of EGA 2. Fetal growth assessment (by US) 3. Amniotic Fluid Index 4. Non-Stress Test 5. Umbilical artery Doppler resistance index or systolic/diastolic ratio

Suspect Preeclampsia?

Hospitalize the patient & do the **initial evaluation** (mentioned above)

Evidence of **severe preeclampsia** or **fetal compromise**?

No

Only observation & monitoring

(monitor: symptoms + BP + weekly laboratory test + fetal activity + NST + AFI)

Deliver when she reaches ≥37 or earlier if she develops signs or symptoms of worsening disease or if there is evidence of fetal compromise.

Yes

Depend on EGA

> 34 weeks

Brief period of Stabilization → Delivery (usually vaginal)

< 34 weeks

The decision regarding delivery needs to be individualized after carefully considering the risks to the neonate of prematurity versus the potential maternal and fetal risks of continuing the pregnancy.

But in general:

1. Stabilise by ($MgSO_4$ + antihypertensive drug/s + Corticosteroid)
2. Monitoring repeated daily until she reach 34 weeks

then:

3. Induce delivery

Summary (Hacker's & Moore's)

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$MgSO_4$ (Seizure prophylactic)

Patients at high risk of seizure	• Patients with preeclampsia • Severe headaches • Visual changes • Sustained clonus • Positive Chvostek sign
Benefit	Prevention and treatment of eclamptic seizures.
Administration	Should be administered in all 3 stages: 1. In the **initial** period of stabilization 2. **Intrapartum** 3. 24h **postpartum** (or until there is evidence of resolution of the disease.)
Route of administration	• IV (better) or IM. • Administration of loading dose of 5g IV over 20 min, and maintenance infusion at 2g/hr which is halved when oliguria or serum Cr ≥1.1) • Therapeutic range: 4.8 - 9.6 mg/dl but, to avoid toxicity, levels should not be allowed to rise above 7 to 8 mg/dL.

Precautions	• Low- dose aspirin (60 to 80 mg/day beginning at the end of the first trimester) for women with a history of recurrent preeclampsia or severe preterm preeclampsia.
	• **Assessment of:**
	  ○ Urine output because magnesium ion is excreted exclusively through the kidneys
	  ○ Deep tendon reflex (e.g patellar reflex)
	  ○ Respiration
	  ○ Arterial oxygen saturation
	  ○ Measurement of serum MgSO4 levels every 6h (2h if there was signs of renal impairment; oliguria or Cr≥1.1)

$MgSO_4$ toxicity	TABLE 14-2 **CLINICAL CORRELATES OF SERUM MAGNESIUM SULFATE LEVELS** Clinical Response — Serum Levels* (mg/dL) Loss of patellar reflex — 8-12 Warmth and flushing — 9-12 Somnolence — 10-12 Slurred speech — 10-12 Paralysis and respiratory difficulty — 15-17 Cardiac arrest — 30-35 *Therapeutic range: 4.8-9.6 mg/dL. **Treatment:** 1. Stop the infusion 2. 10 ml of 10% IV Ca gluconate (if severe)

Summary (Meded)

	Transient HTN Can come to pregnant or non pregnant patient	Chronic HTN (usually know about it before pregnancy	Gestational HTN	Preeclampsia Without Severe Features (PEC)	old name (mild pre-eclampsia)	Preeclampsia With Severe Features (SPEC)	(old name (severe pre-eclampsia)	Eclampsia
Blood Pressure	=>140/80 Only one reading to make the diagnosis	=>140/80	=>140/80	=>140/80	=>160/110 mmHg	-
Timing Of Onset	Non sustained elevation in BP	Sustained elevation in BP with onset before 20 weeks	Sustained elevation in BP with onset after 20 weeks	Sustained elevation in BP with onset after 20 weeks	Sustained elevation in BP with onset after 20 weeks	Sustained elevation in BP with onset after 20 weeks
Urine Analysis	-	-	-	Proteinuria >300 mg/dL	Severe Proteinuria > 5 g/dL	-
Alarm Symptoms	-	-	-	-	Present	Active seizures
Treatment	-	Alpha-methyldopa (best) Labetalol hydralazine	-	At term : >37 weeks = deliver Not term <37 weeks= wait	Give MgSO4 and deliver , age is irrelevant : usually vaginally by induction	Give MgSO4 and deliver , age is irrelevant : usually emergency C-section
Follow Up	Ambulatory BP monitoring (log)	Close monitoring Frequent assessment U/A US	Can progress to pre-eclampsia Close monitoring U/A US Frequent assessment	More frequent follow ups (weekly) Continuous Screen for alarm symptoms and worsening of proteinuria	-	-

(MedEd Notes)

Introduction: Hypertensive disorders in pregnant women are not good for baby or mom. It's one of the largest sources of maternal/fetal morbidity and mortality world-wide. Hypertension comes in 5 categories.

1)Transient Hypertension (tHTN)
Just like normal patients, pregnant women can have a high blood pressure because they get nervous (anxiety or white coat hypertension) or due to exercise (running to the office because she was late). So, if a hypertensive patient is discovered (> 140 / >90) the first thing to do is just let her relax and recheck it (same visit). In a medicine patient we wait two weeks and recheck. However, hypertension in a pregnant woman over 20 weeks gestation can be more than just hypertension, so we SHOULD get a urinalysis (rule out proteinuria) and have her keep a log (i.e ambulatory blood pressure monitoring).

2)Chronic Hypertension (cHTN)
Any sustained hypertension for any reason before 20 weeks is cHTN.
Hypertension that predates the pregnancy. This is defined as blood pressures of > 140 / > 90 before 20 weeks. It can complicate things. Absolute pressures can no longer be used to identify PreE. cHTN is covered further in Ob: Medical disease. Control the blood pressure with α-methyldopa (test answer), hydralazine, or labetalol. Because blood pressure can no longer be used, a close follow-up (urinalysis for protein and ultrasound for intrauterine growth restriction) must be maintained.

3)Gestational HTN
Any sustained hypertension after 20 weeks is gHTN... unless it gets worse and progresses to Preeclampsia spectrum
Elevated BP after 20 weeks in the absence of proteinuria or the other systemic findings of preeclampsia. This is someone who has the elevated pressures, but never crosses the threshold to PreE.

4)Preeclampsia with and without severe features
The old terms mild PreE and severe PreE have been replaced to emphasize both the pathology of disease and the continuum of a spectrum. What was taught was "PreE = HTN + Proteinuria... and look for alarm symptoms." This was simple, but there was re-emphasis on the fact that mom could be nearing full-blown Eclampsia even without proteinuria if she has all the other signs. The point is PEC with severe features implies an increased severity if any ONE of the alarm symptoms are present, and the more of them there are, the worse it is.
PEC is defined as a blood pressure > 140 / > 90 and proteinuria 300 mg/dL. If all you had was the BP, it would count only as gHTN. PEC with severe features is defined as "worse than PEC" and "has any one feature" of severe BP, severe proteinuria, or alarm symptoms. Eclampsia is defined by seizure activity. You should always treat hypertension. This is done with anti- hypertensive agents labetalol or hydralazine. Think of this as inpatient IV management while mom is observed.
Magnesium is both anti-hypertensive and anti-epileptic. It isn't needed in PEC, but is indicated in both sPEC and EC. Magnesium is given during labor and 24 hours after delivery. Magnesium infusion causes hypotension (we wanted that - antihypertension), and relaxation of all nerves (we want that too - anticonvulsant). But too much mag can cause relaxation of important nerves (respiratory failure) and eventual cardiac arrest. Mag checks are performed to assess for a reduced respiratory rate and loss of deep tendon reflexes. These are the earliest signs of magnesium toxicity. Calcium is used as the reversal agent for too low a magnesium.
Delivery and the method to deliver is determined by age and severity. The actual decision to induce versus C-section is dependent on mom and baby's stability, the gestational age, a risk-benefit assessment on more time in the oven, steroids, development, and risk of death. We teach here a 1:1 correlation of disease:treatment because it's easier to understand as an M3 than disease-severity:treatment-severity. In reality, not all sPEC is sPEC (it's a spectrum). On the USMLE Step 2, and for those not going into Obstetrics, this table is sufficient. The main point is that delivery is the only cure for PEC-sPEC-EC spectrum.

5)Superimposed HTN on PEC
When someone with cHTN develops PEC. Since the USMLE step 2 has no curveballs, just recognize this is a thing. You can't be tested on it. It's also why there is MFM training beyond OB residency.

Nomenclature

Old Way		The New Way	
Mild PreEclampsia	Mild PreE	Preeclampsia without severe features	PEC
Severe PreEclampsia	Severe PreE	Preeclampsia with severe features	sPEC

PEC without and PEC with severe features

PEC	Severe Features (any one)
BP ≥ 140 / ≥ 90 and onset after 20 weeks and Proteinuria ≥ 300mg/dL Continue pregnancy until 37 weeks then deliver	1. BP ≥ 160 / ≥ 110 2. Cr ≥ 1.1 or 2x baseline 3. Plt < 100 4. ↑ AST or ALT 2x ULN 5. RUQ or Epigastric Pain 6. Pulmonary Edema 7. Headache or Visual Disturbance Magnesium and Urgent Delivery

Treating Eclampsia Spectrum

HTN	*Magnesium*	*"Anti-Epileptics"*
Labetalol Hydralazine	During Labor And	Benzos to abort
	24 hrs p delivery	Magnesium
	Mag Checks*	Delivery

Treatment based on Severity

Dz	*Control BP*	*Mag*	*Deliver*
PEC	Yes	No	> 37 wks electively < 37 wks observe
sPEC	Yes	Yes	Urgently – Induction*
EC	Yes	Yes	Emergently – Section*

**the choice between induction and section depend not on the diagnosis, but on stability. Memorize this table for the test.*

Benefit of Time by Gestational Age (Ballpark)

Age	*Term*	*Benefit to Baby*
> 37 weeks	Term	None – normal baby
34-37 weeks	Near term	Small
24-34 weeks	Premature	Large
20-24 weeks	Nonviable	None – dead baby
< 20 weeks	Abortion	None – dead baby

Risk to mom is more easily assessed by the presence of severe features. Risk/benefit to baby is based more on gestational age – will more time in the oven be worth the risk to mom? DON'T MEMORIZE THIS FOR THE TEST

	Blood Pressure	*Timing*	*Urine*	*Symptoms*	*Treatment*
Transient HTN	≥140 / ≥90	Unsustained any time	ø	ø	Conservative **Keep a Log**
Chronic HTN	≥140 / ≥90	Sustained, Starting **before 20 weeks**	ø	ø	**α-methyldopa** Hydralazine Labetalol
Gestational HTN	≥140 / ≥90	Sustained, Starting **after 20 weeks**	ø	ø	**Monitor** for PEC
PEC	**≥ 140 / ≥90**	Sustained, Starting **after 20 weeks**	**> 300mg/dL** proteinuria	ø	> 37 weeks **deliver** urgently (induced) < 37 weeks **bed rest**
sPEC	**> 160 / > 110**	Sustained, Starting **after 20 weeks**	+/- **proteinuria**	Positive*	**Mag + BP** + deliver urgently (Induced)
Eclampsia	----------	----------	----------	**Seizures**	**Mag + Deliver** emergently (Section)
HELLP	Hemolysis	Elevated LFTs	Low	Platelets	**Mag + Deliver** emergently (Section)

Reference

Hypertensive Disorders of Pregnancy

LONY C. CASTRO • CALVIN J. HOBEL

CLINICAL KEYS FOR THIS CHAPTER

- Preeclampsia (sometimes called *toxemia of pregnancy*) is a multisystem disorder that is thought to arise as a consequence of inadequate cytotrophoblastic invasion of the spiral uterine arteries and failure to establish the normal low resistance uteroplacental circulation. This leads to placental ischemia and the presumptive involvement of secondary mediators responsible for endothelial dysfunction, local and systemic vasospasm, and activation of the coagulation system. Clinical manifestations of preeclampsia reflect this pathophysiology, and the disease begins to resolve with the delivery of the placenta.
- The diagnosis of preeclampsia is based on the presence of new-onset hypertension after 20 weeks' gestation, accompanied by new onset of proteinuria. When evaluating a pregnant woman with new-onset hypertension without proteinuria, preeclampsia can also be diagnosed if there is evidence of one or more of the following abnormalities: thrombocytopenia or disseminated intravascular coagulation (DIC), elevated transaminases or other signs of hepatic injury, central nervous system (CNS) symptoms, an elevated or rising serum creatinine level, or pulmonary edema (Box 14-1).
- Severe hypertension (systolic blood pressure ≥160 mm Hg and/or diastolic blood pressure ≥110 mm Hg) in the setting of preeclampsia requires rapid blood pressure control, usually with parenteral labetalol or hydralazine to prevent CNS hemorrhage or stroke. When preeclampsia is accompanied by new-onset grand mal seizures, it becomes eclampsia. Eclampsia can result in major maternal morbidity, including intracerebral hemorrhage, placental abruption, and preterm birth or fetal death.
- The diagnosis of chronic hypertension requires at least either known hypertension before pregnancy or the development of hypertension before 20 weeks' gestation. Chronic hypertension is generally not treated in pregnancy unless the blood pressure is ≥160/105 mm Hg. Superimposed preeclampsia is diagnosed by the detection of new-onset proteinuria or the development of signs of severe preeclampsia after 20 weeks' gestation in a pregnant woman with chronic hypertension. Management of superimposed preeclampsia is similar to that outlined for preeclampsia.
- *Gestational hypertension* refers to the development of elevated blood pressure without proteinuria or other signs of preeclampsia after 20 weeks' gestation or within 72 hours of delivery that resolves by 12 weeks postpartum. These women must be followed closely, because a significant percentage will go on to develop preeclampsia in the current pregnancy or in a subsequent pregnancy.

The hypertensive disorders of pregnancy (including preeclampsia/eclampsia, chronic hypertension, superimposed preeclampsia, and gestational hypertension) are important contributors to maternal and perinatal morbidity and mortality. The worldwide incidence of these disorders is reported to be about 10%, but regional estimates vary, depending on the population being studied and on the criteria used for diagnosis. Preeclampsia is most easily recognized in pregnant women who present with the "classic triad" of new-onset hypertension, proteinuria, and edema in the latter half of pregnancy. However, this is only one of the ways in which this multisystem disorder can present. Both the mother with preeclampsia and the fetus carried in an affected pregnancy can present with significant multisystem disorders and complications.

The Centers for Disease Control and Prevention states that preeclampsia/eclampsia is one of the leading causes of maternal mortality in the United States. The mortality is primarily due to central

BOX 14-1
CRITERIA FOR SEVERE PREECLAMPSIA

- Severe hypertension (systolic BP ≥160 mm Hg or diastolic BP ≥110 mm Hg) at rest on two occasions at least 4 hr apart*
- Renal insufficiency (serum Cr >1.1 mg/dL or doubling of baseline values)
- Cerebral or visual disturbances
- Pulmonary edema
- Epigastric or right upper quadrant pain
- Elevated liver enzymes (AST or ALT at least two times normal level)
- Thrombocytopenia (platelet count <100,000/μL)

Based on the American College of Obstetricians and Gynecologists Executive Summary: Hypertension in pregnancy, 2013.
ALT, Serum alanine aminotransferase; *AST*, serum aspartate aminotransferase; *BP*, blood pressure; *Cr*, creatinine.
*4-hr delay not required if antihypertensive therapy is initiated.

BOX 14-2
GENERAL CLASSIFICATION OF HYPERTENSIVE DISORDERS OF PREGNANCY

- Preeclampsia/eclampsia
- Chronic hypertension
- Chronic hypertension with superimposed preeclampsia
- Gestational hypertension

Based on the American College of Obstetricians and Gynecologists Executive Summary: Hypertension in pregnancy, 2013.

nervous system (CNS) hemorrhage. Because of this concern, there is an increased emphasis on the use of standardized practice guidelines to manage patients with preeclampsia and other hypertensive disorders, with the aim of decreasing the maternal and perinatal morbidity and mortality that accompany them.

Classification and Definitions

The general classification of hypertensive disorders recommended in 2013 by the American College of Obstetricians and Gynecologists (ACOG) Task Force on Hypertension in Pregnancy reaffirmed the previous classification of hypertensive disorders used in the Working Group on High Blood Pressure in Pregnancy issued in 2000 (Box 14-2).

Blood pressure readings vary, depending on maternal position and the gestational age of the pregnancy. Maternal blood pressure tends to be lower in the left lateral decubitus position and higher in the sitting position. In the supine position, some pregnant women will have elevated pressure, whereas others will have supine hypotension due to compression of the vena cava by the uterus. In addition to positional variations, arterial blood pressure normally declines during the first and second trimesters of pregnancy and rises to prepregnancy levels in the third trimester.

The diagnosis of hypertension should be reserved for pregnant women with a systolic blood pressure ≥140 mm Hg and/or a diastolic blood pressure ≥90 mm Hg. Blood pressure measurements should be taken with the woman in the sitting position after she has rested ≥10 minutes if she is ambulatory. In the hospitalized patient, either sitting or lateral decubitus measurements may be used; however, measurements should be corrected to the level of the right atrium, and consistency of measurement is advised. The length of the blood pressure cuff should be ≥1.5 times the circumference of the upper arm and the fifth Korotkoff sound (disappearance) should be used for the determination of diastolic pressure.

PREECLAMPSIA/ECLAMPSIA

Preeclampsia is a multisystem disorder unique to pregnancy and has varying clinical presentations. The diagnosis is based on the presence of new-onset hypertension in the latter half of gestation, accompanied by new-onset proteinuria and/or other evidence of organ dysfunction. When evaluating a pregnant woman with new-onset hypertension who does not have proteinuria, preeclampsia can be diagnosed if there is evidence of one or more of the following abnormalities: thrombocytopenia or disseminated intravascular coagulation (DIC), elevated transaminases or other signs of hepatic injury, CNS symptoms, an elevated or rising serum creatinine level, or pulmonary edema. Hypertension is classified as mild or severe. It is a disease affecting the first pregnancy, but it also occurs in multiparas, especially if there are predisposing risk factors (see discussion of pathogenesis and risk factors below). Box 14-1 lists the criteria for diagnosing severe preeclampsia.

***New-onset hypertension* is defined as the development of hypertension** (systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg on two occasions 4 hours apart) **in a woman whose blood pressure readings were previously normal, after the 20th week of pregnancy.** ***New-onset proteinuria* is defined as ≥0.3 g of protein in a timed 24-hour urine collection or a protein/creatinine ratio ≥0.3 after the 20th week of gestation.** This usually correlates with a urinalysis result of ≥30 mg/dL (1+ on dipstick) on a clean-catch urine sample. At each prenatal clinic visit, a pregnant woman's blood pressure, weight, and dipstick urinalysis should be recorded, and she should be assessed for edema. **Rising blood pressures should be of concern,** because they may precede the development of the full preeclamptic syndrome. Similarly, **preeclampsia is often preceded by, or associated with, the development of generalized edema.** Dependent edema (edema of the lower extremities) is very common in normal pregnancies. Hand and facial edema are more likely to be associated with preeclampsia, but they are not diagnostic of the preeclamptic syndrome.

Preeclampsia is often a progressive disease and may have severe features, depending on the severity of the hypertension and the degree to which other organ systems are affected. **Box 14-1 lists specific criteria for the diagnosis of severe preeclampsia.** If any of the symptoms, signs, or laboratory abnormalities listed in Box 14-1 are present in a woman with preeclampsia, it is very likely that she has severe disease, which is associated with much greater maternal and perinatal morbidity.

A variant of severe preeclampsia with particularly high morbidity is the HELLP syndrome. This syndrome occurs in preeclamptic women with evidence of *h*emolysis, elevated *l*iver enzymes, and *l*ow *p*latelets (thrombocytopenia). In contrast to more typical presentations of preeclampsia, the patient with HELLP syndrome is more likely to be multiparous, older than 25 years of age, and at less than 36 weeks' gestation. Hypertension may be initially absent in 20% of the patients, whereas 30% will have mild elevations in blood pressure and 50% will have severe elevations.

ECLAMPSIA

Eclampsia is the presence of new-onset grand mal seizures in a woman with preeclampsia that cannot be attributed to other causes. Patients with severe preeclampsia, especially those with CNS symptoms, are at the greatest risk of developing seizures, but the seizures can occur in patients with preeclampsia without other evidence of severe disease. **There is a wide range in the severity and timing of eclamptic grand mal seizures. Clinical practices,** including the use of magnesium sulfate intrapartum and postpartum for seizure prophylaxis in women with preeclampsia, as well as the timely recognition and delivery of women with severe preeclampsia, undoubtedly **influence these numbers. In one review of this subject, 38–53% of eclamptic seizures occurred before labor, 18–36% occurred during labor, and 11–44% occurred after delivery** (usually within the first 24 to 48 hours). When evaluating atypical cases of eclampsia (i.e., more than 48 hours postpartum or previous evidence of only mild disease), it is important to consider other causes of seizures, such as underlying seizure disorder; hypertensive encephalopathy; metabolic abnormalities, including hypoglycemia and hyponatremia; and CNS hemorrhage, thrombosis, tumor, or infection.

CHRONIC HYPERTENSION

The diagnosis of chronic hypertension requires at least one of the following: known hypertension before pregnancy or the development of hypertension before 20 weeks' gestation.

Most pregnant women with chronic hypertension will have essential hypertension, but **a small percentage will have secondary hypertension** that has renal, vascular, endocrinologic, or behavioral causes (e.g., methamphetamine and cocaine use). Most of these conditions can be suspected on the basis of a thorough history and physical examination. Certain endocrinologic disorders, in particular hyperthyroidism, may present for the first time during pregnancy. Depending on the associated symptoms, signs, and response to medication, a workup to determine the etiology of the hypertension may be indicated. **It is not uncommon for the physiologic stress of pregnancy to cause subclinical vascular or renal disease to become manifest.** In these situations, it may be very difficult to differentiate between preeclampsia and an aggravated chronic hypertensive condition. Sometimes only careful postpartum follow-up will indicate the correct diagnosis.

CHRONIC HYPERTENSION WITH SUPERIMPOSED PREECLAMPSIA

Preeclampsia may become superimposed on chronic hypertensive disease. Superimposed preeclampsia can be very difficult to distinguish from poorly controlled chronic hypertension, especially if the woman is not seen until after the 20th week of gestation, but the two conditions are managed differently. In general, superimposed preeclampsia carries a worse prognosis than either condition alone.

The diagnosis of superimposed preeclampsia should be reserved for those women with chronic hypertension who develop *new-onset proteinuria* (≥0.3 g in a 24-hour collection) after the 20th week of gestation. In pregnant women with preexisting hypertension and proteinuria, the diagnosis of superimposed preeclampsia should be considered if they experience sudden significant increases in blood pressure or proteinuria or the new-onset of any of the other signs and symptoms of severe preeclampsia listed in Box 14-1, including thrombocytopenia or abnormally elevated liver enzymes.

GESTATIONAL HYPERTENSION

The diagnosis of gestational hypertension is made if hypertension without proteinuria or other signs of organ dysfunction first appears after 20 weeks' gestation or within 48 to 72 hours of delivery and resolves by 12 weeks postpartum. It is extremely difficult to differentiate this condition from the early stages of preeclampsia. These women must be followed closely because a significant percentage go on to develop proteinuria and the full preeclamptic syndrome at a later stage in pregnancy. Others will have previously unrecognized chronic hypertension. **The diagnosis of gestational hypertension can only be made in retrospect, if the pregnancy has been completed without the development of proteinuria or other evidence of preeclampsia, and if the blood pressure has returned to normal before the 12th week postpartum.**

Preeclampsia/Eclampsia

PATHOGENESIS AND RISK FACTORS

Preeclampsia is called a "disease of theories" because genetic, immunologic, vascular, hormonal, nutritional, and behavioral factors have all been proposed as causes. No single, definitive "cause" has been identified and the origins of the disease are considered to be multifactorial. **Because of the resolution of the preeclampsia after delivery, most attention has been focused on the placenta and the uteroplacental-fetal interface.**

Inadequate uteroplacental perfusion leading to placental ischemia, or hypoxia, appears to be central to the development of the disease. This has been attributed to failure of the cytotrophoblasts to adequately invade the uterine spiral arteries and establish the low-resistance uteroplacental circulation characteristic of normal pregnancy. Placental ischemia could also be due to underlying maternal vascular disease. This could explain the well-documented maternal risk factors for preeclampsia, such as chronic hypertension, advanced maternal age, or methamphetamine use. Immunologically mediated placental vascular damage could explain the higher incidence of preeclampsia in primigravidas and in pregnant women with autoimmune disorders such as the antiphospholipid syndrome. Alternatively, ischemia could be caused by increased metabolic demands in the setting of a multiple gestation, a large singleton fetus, or gestational trophoblastic disease. **When preeclampsia arises in the early second trimester (14 to 20 weeks), a hydatidiform mole or choriocarcinoma should be considered. Other as yet poorly defined genetic and environmental factors will likely be identified that explain the high risk of recurrence of preterm preeclampsia in subsequent pregnancies and the familial association (i.e., increased risk in daughters of women with preeclampsia).**

It is postulated that uteroplacental ischemia results in oxidative and inflammatory stress, with the involvement of secondary mediators leading to endothelial dysfunction, vasospasm, and activation of the coagulation system. The nature of these toxins has not yet been identified, but it may involve production of reactive oxygen and nitrogen species. This is supported by the observation that preeclampsia is increased in pregnant women with underlying conditions, such as obesity and diabetes, that are associated with chronic inflammation and dyslipidemia. A hypoxic placenta may also shed microparticles derived from apoptosis of syncytiotrophoblasts, which can then lead to widespread endothelial injury. Antiangiogenic factors have also been shown to cause systemic hypertension, vascular injury, and activation of the coagulation system. Preeclamptic women have an imbalance in angiogenic and antiangiogenic proteins. Circulating levels of the proangiogenic proteins vascular endothelial growth factor and placental growth factor are decreased, whereas levels of the antiangiogenic proteins soluble fms-like tyrosine kinase 1 (sFlt1) and soluble endoglin are markedly increased. In animal models, overexpression of sFlt1 results in a preeclampsia-like syndrome.

Endothelial dysfunction leads to an imbalance between different classes of locally produced vasoconstrictors and vasodilators. Preeclampsia is associated with a disturbance in prostaglandin production, with a decrease in the ratio of the vasodilators prostaglandin E_2 and prostacyclin to the vasoconstrictor $PGF_{2\alpha}$ and thromboxanes. **Endothelial changes also appear to involve a relative deficiency in the production of nitric oxide, a vasodilator and inhibitor of platelet aggregation, along with increased production of endothelin.** Endothelin is an extremely potent vasoconstrictor and activator of platelets. This shift in the production of locally acting vasoactive substances could enhance vasoconstriction in response to circulating pressor hormones.

The net effect of the above-described processes would be widespread vasoconstriction leading to hypoxic/ischemic damage in different vascular beds, systemic hypertension, activation of the coagulation system, and worsening placental ischemia. The relative severity of the signs and symptoms of preeclampsia in any given individual would vary on the basis of which specific organ system was affected.

PATHOLOGY

Three major pathologic lesions are classically associated with preeclampsia and eclampsia: (1) lack of decidualization of the myometrial segments of the spiral arteries; (2) glomerular capillary endotheliosis; and (3) ischemia, hemorrhage, and necrosis in many organs, presumably secondary to arteriolar constriction.

Under normal circumstances, the invasion of trophoblast results in the replacement of the muscular and elastic layers of the spiral arteries by fibrinoid and fibrous tissue, resulting in large, tortuous, low-resistance channels that extend through the myometrium. In preeclampsia, this change is mostly limited to the decidual segments of the vessels and may result in a 60% reduction in the diameter of the myometrial segment of the spiral arteries. **Placental abruption is increased in almost all preeclamptic pregnancies.**

The typical renal lesion of preeclampsia/eclampsia is "glomerular capillary endotheliosis," which is best seen by electron microscopy. This disorder is manifested by marked swelling of the glomerular capillary endothelium and deposits of fibrinoid material in and beneath the endothelial cells. **Arteriolar vasospasm of relatively short duration (1 hour) can cause hypoxia and necrosis of sensitive parenchymal cells.**

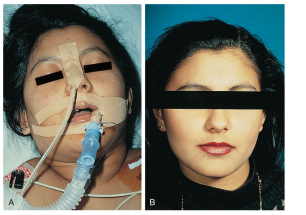

FIGURE 14-1 A postpartum patient after an eclamptic seizure and delivery secondary to severe preeclampsia (**A**). She experienced confusion, severe headache, and loss of vision before the eclamptic seizure. Note the marked facial edema. Because of the patient's loss of vision, the diagnosis of posterior reversible encephalopathy syndrome was assessed by magnetic resonance imaging, which showed segmental vasoconstriction. The cause is related to loss of autoregulation of the cerebral circulation because of vascular endothelial damage and brain edema. The treatment includes prevention of recurrent seizures with magnesium sulfate, aggressive control of hypertension, and reduction of excessive vascular volume by rapid diuresis with furosemide. Note the patient's status at 5 weeks postpartum (**B**). (From Sibai BM: Etiology and management of postpartum hypertension-preeclampsia. *Am J Obstet Gynecol* 206:470–475, 2012.)

Vasospasm of longer duration (3 hours) can lead to infarction of vital organs, such as the liver, placenta, and brain. In the liver, periportal necrosis and hemorrhage may occur, with subcapsular hematoma and hepatic rupture being rare complications. In the brain, focal areas of hemorrhage and necrosis may occur. In the retina (the clinical window to the arterial vasculature), vasospasm may be visualized on ophthalmoscopic examination. **Retinal hemorrhage is considered to be an extremely ominous sign** because it may signal similar phenomena in other vital organs.

CLINICAL AND LABORATORY MANIFESTATIONS

Many of the clinical and laboratory manifestations of preeclampsia discussed below can be explained on the basis of endothelial dysfunction, vasospasm, and activation of the coagulation system. This unifying principle may one day lead to the definitive explanation of the causes of preeclampsia.

Weight Gain and Edema

Abnormal weight gain and edema occur early with preeclampsia and reflect an expansion of the extracellular fluid compartment. This expansion is related to the endothelial injury and increased capillary permeability that allow fluid to diffuse from the intravascular to the extravascular space. Thus, many patients with preeclampsia have an increase in total body fluid volume but have intravascular volume depletion. **The hematocrit may also increase, reflecting the relative hypovolemia and hemoconcentration. These "leaky" capillaries predispose women with preeclampsia to pulmonary edema if they are treated with aggressive volume loading. Diuretic therapy is generally not advised unless there is evidence of pulmonary edema.**

Figure 14-1 shows a preeclamptic woman with fluid retention just before delivery (see Figure 14-1, *A*) and at her postpartum visit 6 weeks after delivery (see Figure 14-1, *B*).

Hypertension

The elevation of blood pressure seen in preeclampsia (particularly the increase in diastolic pressure) is a result of generalized vasospasm and an increase in systemic vascular resistance. The blood pressure changes may occur days to weeks after the onset of pathologic fluid retention. Cardiac output in untreated pregnant patients with preeclampsia is not significantly different from that of normal subjects in the last trimester of pregnancy.

Renal Function

Renal blood flow and glomerular filtration rate (GFR) are significantly lower than in patients with a normal

pregnancy. The decrease in renal blood flow results from constriction of the afferent arteriolar system. **This afferent vasoconstriction may eventually lead to damage to the glomerular membranes, thereby increasing the permeability of these membranes to proteins and leading to proteinuria.** The renal vasoconstriction and decrease in GFR also account for elevations in serum concentrations of creatinine, blood urea nitrogen, and uric acid.

In the antepartum period, proteinuria may occur days or weeks after the onset of hypertension. If the disease first manifests during labor or in the immediate postpartum period, this progression of events is compressed into hours and sometimes minutes. Renal involvement may progress to significant oliguria and frank renal failure.

Coagulation System

Activation of the coagulation system is often clinically apparent with severe disease. **Thrombocytopenia is the most common abnormality.** Although platelet counts tend to decline even in normal pregnancies, a value <100,000 cells/mm³ is clearly pathologic and, if accompanied by other signs of preeclampsia, is evidence of severe disease. DIC may occur, especially if there is a placental abruption. **The specific combination of hemolysis, elevated liver function tests, and low platelet levels (the HELLP syndrome)** can occur without clinical manifestations of DIC and **is a sign of severe preeclampsia,** even if blood pressures are normal or only minimally elevated. Women with preexisting thrombophilias, either acquired or inherited, are at increased risk for developing preeclampsia.

Liver Function

In the liver, vasospasm may result in focal hemorrhages and infarctions leading to right upper quadrant or epigastric pain and elevated serum enzyme levels (alanine aminotransferase and aspartate aminotransferase). Hepatic rupture is a rare, ominous complication of preeclampsia that is usually associated with the HELLP syndrome. When significant hemolysis is present, bilirubin levels are often elevated. Elevated alkaline phosphatase levels are frequently seen in pregnancy and are usually not of clinical significance, as they are mostly due to placental production of this enzyme.

Placental Function

Decreased uteroplacental perfusion and ischemia can lead to fetal compromise in the form of intrauterine growth restriction (IUGR), oligohydramnios, or fetal heart rate abnormalities. A commonly accepted clinical sign of inadequate placental perfusion is an umbilical artery Doppler study revealing absent or reversed umbilical artery end diastolic flow. **Extensive placental infarctions can result in retroplacental hemorrhage, or abruption,** which is an important cause of perinatal morbidity and mortality.

Central Nervous System Effects

Cerebral vascular resistance is high in patients with preeclampsia and eclampsia. In patients with hypertension without convulsions, cerebral blood flow may remain within normal limits as a result of autoregulatory phenomena. In patients with convulsions, however, cerebral blood flow and oxygen consumption are significantly lower. **Visual disturbances** such as blurred vision, spots, and scotomata represent degrees of retinal vasospasm. Sudden loss of vision (cortical blindness) is due to occipital lobe ischemia. If the mother is expeditiously stabilized and delivered, full restoration of vision is likely to occur. **A new-onset headache and increased reflex irritability or hyperreflexia are extremely concerning signs of CNS involvement and may predict imminent seizures.**

Evaluation and Management of Preeclampsia

There are three important questions the clinician must ask when managing a woman with preeclampsia. First, does the disease process have severe features? Second, is there evidence of fetal compromise (i.e., IUGR, oligohydramnios, or heart rate abnormalities)? Third, is the fetus mature enough for a reasonably uncomplicated course after delivery?

Delivery is the only definitive cure for preeclampsia, so it is always beneficial for the mother; however, it may result in the delivery of a very preterm neonate. The goal of management is to decrease or prevent the maternal complications of severe preeclampsia while minimizing the neonatal complications arising from prematurity. A woman with preeclampsia, without evidence of fetal compromise, and whose disease does not appear to be severe or progressing will generally not be delivered unless the gestational age is 37 weeks or older, whereas **a woman with severe preeclampsia or eclampsia whose disease presents at or beyond 34 weeks' gestation will usually be delivered after a brief period of stabilization. Severe preeclampsia presenting at less than 34 weeks' gestation may in certain situations be stabilized with careful monitoring of the mother and fetus, delivery may be delayed until the pregnancy reaches 34 weeks.**

The initial assessment involves a complete medical history, physical examination, and laboratory evaluation. The evaluation should focus on whether there is any past history of elevated blood pressure or renal disease, either before pregnancy or during previous pregnancies. The patient should be questioned carefully regarding symptoms of severe preeclampsia or its complications, including headache, visual

BOX 14-3
INITIAL LABORATORY EVALUATION FOR A PATIENT WITH PREECLAMPSIA

- CBC, platelet count, LDH; if abnormal, order ɪ-dimers, coagulation panel, and smear
- Renal studies: serum BUN creatinine and uric acid, urinalysis, 24-hr urine for protein and creatinine, or protein/creatinine ratio
- Liver function tests: AST, ALT, and bilirubin

ALT, Serum alanine aminotransferase; *AST*, serum aspartate aminotransferase; *BUN*, blood urea nitrogen; *CBC*, complete blood count; *LDH*, lactate dehydrogenase.

changes, nausea, vomiting, abdominal or epigastric pain, and vaginal bleeding. Her medical record should be reviewed to determine when in the current pregnancy her blood pressure started to rise and when proteinuria developed.

The physical examination should be focused on the assessment of blood pressure, weight gain, edema, fundal height, and reflexes, as well as on a qualitative assessment of urinary protein excretion with a dipstick. In addition, findings consistent with severe preeclampsia, such as epigastric or right upper quadrant tenderness, uterine tenderness, and signs of pulmonary edema, should be sought. If there is severe headache or visual symptoms, an ophthalmic examination may be indicated. The initial laboratory studies recommended are outlined in Box 14-3.

A careful fetal evaluation is also indicated. This should begin with an accurate determination of fetal gestational age based on clinical and sonographic data, if available. Fetal ultrasound should be performed to evaluate fetal growth, amniotic fluid index, and the umbilical artery Doppler resistance index or systolic/diastolic ratio. **A nonstress test (NST) should also be done** to determine if there is evidence of acute fetal compromise.

It is generally advisable to hospitalize patients with a presumed diagnosis of preeclampsia to determine the disease's severity and the maternal and fetal status. After the initial evaluation, if there is no evidence of severe preeclampsia or **fetal compromise, management consists of observation with careful monitoring of both the mother and fetus for progression of the disease. There is no evidence that bed rest is helpful,** although some activity restriction may be indicated. Chronic antihypertensive therapy or diuretic therapy does not prevent the progression to severe disease and is not recommended. Depending on the special circumstances surrounding each case, expectant management can be carried out in the hospital or on an outpatient basis. The mother will require frequent reassessment of symptoms and blood pressure, along with weekly laboratory tests. The fetus needs to be followed with monitoring of fetal activity, heart rate reactivity (NST), and amniotic fluid volume. **The patient should be delivered by the time she reaches 37 weeks, or earlier if she develops signs or symptoms of worsening disease or if there is evidence of fetal compromise.**

If the initial evaluation is consistent with the diagnosis of severe preeclampsia, the patient should remain hospitalized for the remainder of the pregnancy. After 34 weeks' gestation, stabilization and delivery are appropriate for most patients. For those patients at less than 34 weeks' gestation who have severe preeclampsia, the decision regarding delivery needs to be individualized after carefully considering the risks to the neonate of prematurity versus the potential maternal and fetal risks of continuing the pregnancy. Both the mother and fetus require very close monitoring with maternal laboratory parameters and fetal assessment testing repeated daily or more often if necessary. **In some instances, initial stabilization of the patient with severe preterm preeclampsia with magnesium sulfate for seizure prophylaxis, along with medical control of severe hypertension and corticosteroids for fetal lung maturity, will moderate the disease process and allow delivery to be delayed in the hopes of enhancing gestational age.** Either a deterioration in clinical status (e.g., uncontrollable hypertension, deteriorating renal function, pulmonary edema, evidence of HELLP syndrome or coagulopathy, worsening liver function, CNS symptoms, abruption, or abnormal fetal testing) or attainment of a gestational age of 34 weeks is an indication for delivery.

INTRAPARTUM MANAGEMENT OF PREECLAMPSIA

Labor should be induced, and vaginal delivery anticipated, in the absence of any obstetric indications for cesarean delivery, such as failure to progress in labor, nonreassuring fetal status, or nonvertex presentation. The mother and fetus must be carefully monitored during labor and delivery. **Two of the most important maternal issues to be dealt with are seizure prophylaxis and control of hypertension.** Other potential maternal problems that may develop include oliguria, pulmonary edema, and thrombocytopenia or the HELLP syndrome.

If the fetus is growth-restricted or if placental abruption occurs, the fetal heart rate tracing may show evidence of late decelerations, bradycardia, or other signs of fetal compromise necessitating cesarean delivery (see Chapter 9). In most instances, epidural anesthesia is the anesthetic of choice for operative delivery or pain relief during labor, unless there is evidence of coagulopathy.

SEIZURE PROPHYLAXIS

Because of the risk of seizures and their attendant morbidity and even mortality, attention must be given to the level of CNS irritability. Peripheral reflexes,

particularly of the patella and ankle, are generally used as determinants of heightened instability. **In patients with preeclampsia, severe headaches, visual changes, sustained clonus, or a positive for Chvostek sign can be prodromal symptoms or signs of eclampsia.**

Seizure prophylaxis with magnesium sulfate should be instituted in patients with severe preeclampsia during the initial period of stabilization and again during the intrapartum period, and it should be continued for 24 hours postpartum or until there is evidence of resolution of the disease. **Randomized controlled trials have confirmed that magnesium sulfate is the agent of choice for the prevention and treatment of eclamptic seizures. It is both efficacious for seizure control and associated with low neonatal morbidity.** Both intramuscular (IM) and intravenous (IV) routes are effective for prophylaxis; however, the IM injections can be very painful, and only the IV route is recommended in the United States.

Table 14-1 outlines the protocols for magnesium administration, and Table 14-2 reviews the relationship between serum magnesium concentrations, clinical response, and signs of toxicity, including loss of patellar reflex, warmth and flushing, somnolence and slurred speech, and, most significantly, paralysis and cardiac arrest. Therapeutic levels are generally accepted to be in the range of 4.8 to 9.6 mg/dL, but, to avoid toxicity, levels should not be allowed to rise above 7 to 8 mg/dL. **The magnesium ion is excreted exclusively through the kidneys, so careful monitoring of urine output is essential.** A magnesium overdose can have severe, even fatal, consequences. Magnesium should be given by a controlled infusion pump with a failsafe mechanism to prevent errors in administration (i.e., inadvertent bolus infusion). **Serial assessments of urine output, deep tendon reflexes, and respirations are important for detecting signs of magnesium toxicity.** These clinical assessments should be supplemented with serial measurements of serum magnesium levels every 6 hours and arterial oxygen saturation via pulse oximetry. In a patient who has oliguria or a serum creatinine ≥1.1, maintenance infusion rates should be halved and serial magnesium levels measured every 2 hours. **Magnesium toxicity can occur even in a patient with apparently normal renal function.** Magnesium toxicity is treated by stopping the infusion and, when severe, administering IV calcium gluconate, 10 mL of a 10% solution, along with resuscitative measures if necessary.

TABLE 14-1
ANTICONVULSIVE MAGNESIUM SULFATE THERAPY

Type of Treatment	IV*	IM
Loading dose in 100 mL of fluid	4-6 g over 15-20 min	5 g in each buttock
Maintenance dose	1-2 g/hr controlled IV	5 g/4 hr infusion

IM, Intramuscular; *IV*, intravenous.
*Only the IV route is recommended in the United States.

TABLE 14-2
CLINICAL CORRELATES OF SERUM MAGNESIUM SULFATE LEVELS

Clinical Response	Serum Levels* (mg/dL)
Loss of patellar reflex	8-12
Warmth and flushing	9-12
Somnolence	10-12
Slurred speech	10-12
Paralysis and respiratory difficulty	15-17
Cardiac arrest	30-35

*Therapeutic range: 4.8-9.6 mg/dL.

ANTIHYPERTENSIVE THERAPY

Arterial blood pressure ≥160 mm Hg systolic or ≥110 mm Hg diastolic must be treated promptly. In the setting of severe preeclampsia, blood pressures reaching these levels represent a hypertensive emergency. In some women with preeclampsia, even elevations of systolic blood pressure in the 150 to 159 mm Hg range require urgent treatment, especially in those women whose previous systolic blood pressures have been in the 90 to 100 mm Hg range and who now have HELLP syndrome or eclampsia.

The goal of antihypertensive therapy in severe preeclampsia is to stabilize the mother by lowering blood pressure carefully to prevent CNS hemorrhage. In general, the blood pressure should not be lowered to normal levels or to <130/80 mm Hg. **Caution must be exercised not to lower the arterial pressure too much or too rapidly, for either may result in a decreased uteroplacental blood flow and fetal distress, which may necessitate an emergency cesarean delivery in an unstable mother.**

The safest, most efficacious drugs for the acute control of severe hypertension complicating preeclampsia are labetalol and hydralazine. Although hydralazine has theoretical advantages over labetalol in that it is a direct vasodilator and does not induce bronchospasm, rapid bolus infusions are potentially more likely to induce precipitous hypotension. In general, either is acceptable, and use of one or the other will be determined by the individual circumstances. Table 14-3 details the dosages, durations of action, and potential complications of these two drugs.

Oral nifedipine has been used successfully, starting at a dose of 10 mg orally and repeated in 20 to 30 minutes if necessary to a maximum dose of 30 mg. **Nifedipine should be used cautiously to avoid hypotension,** particularly when used in conjunction with magnesium sulfate. Because of the potential for a precipitous drop in blood pressure, short-acting nifedipine is generally not advised in this setting.

TABLE 14-3
EMERGENCY PARENTERAL THERAPY FOR SEVERE HYPERTENSION DURING PREGNANCY

Agent	Action	Dose	Side Effects	Comments
Hydralazine	Direct vasodilator	5 mg IV over 1-2 min, then 5-10 mg IV every 20-40 min until blood pressure is 130-150/80-100 mm Hg. If no response after 20-25 mg, switch to another drug. Alternatively, give continuous IV infusion of 0.5-10 mg/hr.	Headache, tachycardia, flushing, vomiting	Increases cardiac output and probably uterine vessel blood flow; has historically been drug of choice for short-term control.
Labetalol hydrochloride	Nonselective α-, β-blocker	Start with 10-20 mg IV bolus. If response is inadequate after 10 min, give 20-80 mg IV every 20-30 min if needed to a maximum dose of 300 mg. Alternatively, give a continuous IV infusion of 1-2 mg/min.	Nausea, vomiting, heart block, bronchoconstriction, dizziness	Current drug of choice in many centers. Avoid if evidence of asthma or acute heart failure.
Nifedipine	Calcium channel blocker	10-20 mg orally; repeat in 30 min if inadequate response, then 10-20 mg every 2-6 hours if needed to lower blood pressure to 130-150/80-100 mm Hg.	Reflex tachycardia and headaches	

Modification of the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VII), 2004, Tables 21 and 23.
IV, Intravenous.

MANAGEMENT OF FLUID BALANCE

Accurately recorded intake and output data must be kept to calculate fluid requirements. **Patients with preeclampsia experience vasoconstriction, have interstitial edema, and often demonstrate some degree of reduced intravascular volume, which may reduce urinary output.** In addition, they may be receiving several different therapeutic infusions, such as magnesium sulfate and oxytocin, which have a direct or indirect effect on urinary output.

The most common errors that occur in the management of these patients are fluid volume overload, resulting in pulmonary edema, and excessive volume restriction. Water intoxication is rare with current management. The conservative approach is to replace documented output plus insensible loss with an appropriate electrolyte-containing fluid. Because of the multifaceted pathophysiology of this disease, central hemodynamic monitoring using a pulmonary artery catheter may aid in the management of refractory cases of oliguria or pulmonary edema.

MANAGEMENT OF ECLAMPSIA

Eclampsia is a true obstetric emergency, and all physicians involved in the care of pregnant women should be prepared to recognize an eclamptic seizure and begin initial resuscitative/stabilization efforts. The management of these patients should be carried out by a team of physicians and well-trained nurses in an isolated labor room, with minimal noise and not too much light. As with any seizure condition, the initial requirement is to protect the patient from injury, clear the airway, and give oxygen by face mask to relieve hypoxia. Blood pressure and pulse oximetry should be recorded every 10 minutes with the patient in the lateral position. A 16- to 18-gauge IV line should be placed for drawing blood and administering drugs and fluids. An indwelling catheter should be placed in the bladder, and laboratory tests should be performed as outlined in Box 14-3.

Pharmacologic stabilization consists of preventing recurrent convulsions and controlling hypertension. Randomized controlled trials have confirmed that magnesium sulfate is the most efficacious drug for preventing recurrent eclamptic seizures and has the best safety profile for the mother and fetus. The administration of IV magnesium sulfate for the treatment of eclamptic seizures is similar to its prophylactic use as outlined in Table 14-1, except that the loading dose is generally increased from 4 to 6 g. The maintenance dose remains 2 g/hr if renal function appears normal. If diazepam (Valium) is used in addition to magnesium sulfate, personnel skilled in intubation should be readily available in case maternal respiratory

Reference

depression occurs. In general, it is desirable to avoid polypharmacy.

Eclamptic seizures often induce a fetal bradycardia that usually resolves after maternal stabilization and correction of hypoxia, unless there is a placental abruption. It is very important to stabilize the mother before any attempt is made to deliver the infant. Induction of labor or performing a cesarean delivery during the acute phase may aggravate the course of the disease. **Once hypoxia has been corrected, convulsions controlled, and the diastolic blood pressures brought down to the 90 to 100 mm Hg range, delivery should be expedited, preferably by the vaginal route.**

Currently, there is no scientifically proven method for the prevention of preeclampsia that is applicable to the general population of pregnant women. Low-dose aspirin (60 to 80 mg/day beginning at the end of the first trimester) has been studied extensively in over 30,000 women. Its use is currently advised by the ACOG Task Force for women with a history of recurrent preeclampsia or severe preterm preeclampsia, but the risk reduction is likely to be small. Although nutritional interventions have a sound theoretical and experimental basis, it is likely that dietary modifications and weight reduction will have to be implemented before conception in order to be successful. **The current goal is to identify the disease early, monitor its effects on the mother and fetus, stabilize the patient if the disease is severe, and deliver the baby before there is major disease-induced maternal or fetal morbidity.**

MANAGEMENT OF CHRONIC HYPERTENSION

The primary goals of management of chronic hypertension are to control hypertension and detect the development of superimposed preeclampsia in the mother and IUGR in the fetus. In the patient with uncomplicated hypertension whose blood pressures are well controlled and who does not show signs of superimposed preeclampsia or IUGR, the outcome for both the mother and fetus should be good.

When a woman with chronic hypertension is first seen during her pregnancy, it is important to review previous records to determine whether she has essential hypertension or a secondary cause of high blood pressure. If no previous evaluations have been done, it may be appropriate to rule out some of the more common endocrinologic, renal, or cardiovascular causes of hypertension. Baseline laboratory tests similar to those outlined in Box 14-3, with the addition of an electrocardiogram, may be useful. The purpose of these tests is to establish a baseline should the patient later develop superimposed preeclampsia, as well as to look for evidence of end organ dysfunction.

It is important to review the antihypertensive medications being taken and to discontinue any that are potentially teratogenic. **The ACOG Task Force recommends starting antihypertensive therapy if the systolic blood pressure is ≥160 mm Hg or the diastolic blood pressure is ≥105 mm Hg. There is little evidence that lowering blood pressure below the 140/90 mm Hg range benefits the pregnancy.** In fact, lowering the blood pressure too much may result in decreased uterine perfusion pressure and iatrogenic fetal growth restriction. **In many women, blood pressures will decrease to normal in the second trimester, and no antihypertensive medication will be needed.**

As a general rule, the safest antihypertensive medication should be used at the lowest possible dose needed to keep blood pressure at about 130/80 mm Hg to 140/90 mm Hg. **Methyldopa** is considered to be the safest antihypertensive medication in pregnancy, but **calcium channel blockers** and **labetalol** are also considered to be safe. **Angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, renin inhibitors, and mineralocorticoid blockers should be avoided at all stages of pregnancy because of potential fetal toxicity.** Beta blockers should be used with caution because they may cause fetal growth restriction and may affect the interpretation of the NST. The risks and benefits of moderate exercise (e.g., walking) or increased periods of rest in the left lateral decubitus position have not been well defined, although they are often recommended.

Because these pregnancies have a high incidence of IUGR, both early and serial ultrasonic examinations are indicated. The early ultrasound (before 12 weeks) is primarily for dating, and the 18- to 22-week ultrasound is for the assessment of fetal anomalies. Serial ultrasonic examinations (every 3 to 4 weeks after 26 to 28 weeks) are of great assistance in detecting IUGR. Depending on the clinical circumstances, periodic fetal monitoring with NSTs and amniotic fluid assessment, supplemented by umbilical artery Doppler studies if there is evidence of IUGR or preeclampsia, may be initiated as early as 26 to 28 weeks and should be commenced by 32 to 34 weeks in all patients with hypertension. **Maternal detection of daily fetal kick counts by the mother in the third trimester** or earlier is an important method of assessing fetal well-being.

A significant increase in hypertension or the development of proteinuria in a previously nonproteinuric patient with chronic hypertension is a likely sign of superimposed preeclampsia. The incidence of superimposed preeclampsia varies from 15-25%. These patients should undergo repeat laboratory evaluation, as outlined in Box 14-3. Management should follow that outlined for severe preeclampsia.

The timing of delivery in the patient with chronic hypertension depends on the clinical circumstances. **For patients without evidence of fetal growth restriction or superimposed preeclampsia, in whom blood pressure is well controlled and who have no other indications for delivery, pregnancy may be allowed to progress until at least 38 weeks' gestation, provided that fetal well-being is normal.** Any progression beyond the 40th week should be very carefully considered and probably avoided. The presence of IUGR, blood pressure deterioration, or the advent of proteinuria may dictate earlier delivery. **The route of delivery should be vaginal in the absence of other obstetric reasons for cesarean delivery.**

Sequelae and Outcomes

Women with a history of severe preterm preeclampsia are at high risk for recurrent preeclampsia (up to 40%) in a subsequent pregnancy and are the ones most likely to benefit from prepregnancy lifestyle interventions or antepartum use of low-dose aspirin. There is increasing evidence that a history of preeclampsia raises a woman's risk for cardiovascular disease in later life as compared with women who do not experience preeclampsia. Women with gestational hypertension also seem to have a higher incidence of chronic hypertension later in life. **The female offspring of women with preeclampsia experience an increased risk of preeclampsia in their own pregnancies,** providing evidence of a genetic basis for the disease.

Some of the more serious complications of preeclampsia, such as cerebrovascular accidents and renal failure, may have long-term maternal sequelae. Overall, the mortality rate of women with hypertensive disease of pregnancy varies according to the severity of the disease, socioeconomic level, and quality of care received. Although at present there is no proven way of preventing preeclampsia, accessible, high-quality prenatal care should prevent the majority of severe complications associated with the disease.

Fetal and neonatal sequelae are more difficult to determine, because some of the morbidity and mortality associated with these hypertensive syndromes are related to IUGR, prematurity, and acute and chronic fetal distress. All of these may have long-term CNS and cardiovascular effects.

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