Managing Hypertensive Crisis from Preeclampsia

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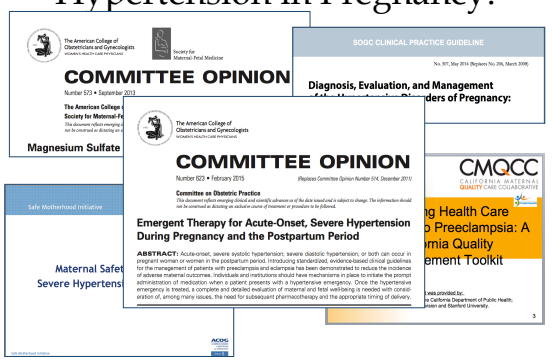
Hypertension in Pregnancy!



Task Force on Hypertension in Pregnancy

New!

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

Hypertension in Pregnancy

Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy

Executive Summary

Obstetrics & Gynecology, November 2013, Volume 122, No.5

New!

CMQCC
CALIFORNIA MATERNAL QUALITY CARE COLLABORATIVE
PublicHealth

Improving Health Care Response to Preeclampsia: A California Quality Improvement Toolkit

CMQCC PREECLAMPSIA TOOLKIT/PREECLAMPSIA CARE GUIDELINES CDPH-MCAH Approved: 12/20/13

Available online at www.cmqcc.org

New!

Why is it important?

New!
CMQCC
CALIFORNIA MATERNAL QUALITY CARE COLLABORATIVE

- Complicates 10% pregnancies worldwide
- One of the greatest causes of maternal & perinatal morbidity and mortality
- ≈ 50,000 – 60,000 preeclampsia –related deaths per year worldwide
- In the US:
  - ➢ Incidence has increased 25% in US during past 20 yrs
  - ➢ For every death from preeclampsia, 50 – 100 women have "near miss" events, significant health risks and costs

Grouped Cause of Death 2002-2004 (N=145)

PublicHealth
CMQCC

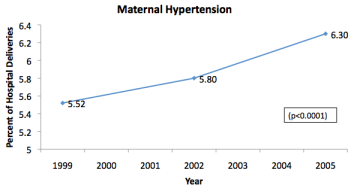
California Pregnancy-Associated Mortality Review (CA-PAMR)
Quality Improvement Review Cycle

Grouped Cause of Death	Chance to Alter Outcome			
	Strong /Good (%)	Some(%)	None (%)	Total N (%)
Obstetric hemorrhage	69	25	6	16 (11)
Deep vein thrombosis/ pulmonary embolism	53	40	7	15 (10)
Sepsis/infection	50	40	10	10 (7)
Preeclampsia/eclampsia	**50**	**50**	**0**	**25 (17)**
Cardiomyopathy & other cardiovascular causes	25	61	14	28 (19)
Cerebral vascular accident	22	0	78	9 (6)
Amniotic fluid embolism	0	87	13	15 (10)
All other causes of death	46	46	8	26 (18)

Maternal Mortality Rate, California Residents; 1970-2010

Maternal Hypertension in California, 1999-2005

Maternal hypertension identified at time of hospitalization for labor and delivery (includes pre-gestational and gestational hypertension)



Source: http://www.cdph.ca.gov/programs/mcah/Documents/MO-CAPAMRTrendsinMaternalMorbidityinCalifornia-1999-2005-TechnicalReport.pdf

How Do Women Die Of Preeclampsia in CA?

CA-PAMR Final Cause of Death Among Preeclampsia Cases, 2002-2004 (n=25)

Final Cause of Death	Number	%	Rate/100,000
• Stroke	16	64%	1
Hemorrhagic	14	87.5%	
Thrombotic	2	12.5%	
• Hepatic (liver) Failure	4	16.0%	.25
• Cardiac Failure	2	8.0%	
• Hemorrhage/DIC	1	4.0%	
• Multi-organ failure	1	4.0%	
• ARDS	1	4.0%	

New!

Why is it important? (Cont.)

- Many Preeclamptic deaths in US and worldwide reported as "preventable"
- Major contributor to prematurity
- Risk factor for future CV disease and metabolic disease in women
- Etiology remains unclear
- The only cure is delivery (of the placenta)

New!

Management Issues Warranting Special Attention

- Failure of healthcare providers to appreciate the multi-systemic nature of preeclampsia
- Preeclampsia is a dynamic and a progressive process
  1. Appropriate management mandates frequent reevaluation
  2. Can worsen or present after delivery – which can create a venue for adverse maternal events

New!

ACOG Executive Summary on Hypertension In Pregnancy, Nov 2013

1. The term "mild" preeclampsia is discouraged for clinical classification. The recommended terminology is:
   a. **"preeclampsia without severe features" (mild)**
   b. **"preeclampsia with severe features" (severe)**
2. Proteinuria **is not a requirement to diagnose preeclampsia** with **new onset hypertension.**
3. The **total amount of proteinuria > 5g in 24 hours has been** eliminated from the diagnosis of severe preeclampsia.
4. **Early treatment of severe hypertension is mandatory at the** threshold levels of **160 mm Hg systolic or 110 mm Hg** diastolic.

New!

ACOG Executive Summary on Hypertension In Pregnancy, Nov 2013 (cont.)

5. Magnesium sulfate for seizure prophylaxis is **indicated for severe preeclampsia and should not be administered** universally for preeclampsia without severe features (mild).
6. Preeclampsia with onset **prior to 34 weeks is most often severe and should be managed at a facility with appropriate** resources for management of serious maternal **and neonatal** complications.
7. Induction of labor **at 37 weeks is indicated for preeclampsia and gestational hypertension.**

New!

ACOG Executive Summary on Hypertension In Pregnancy, Nov 2013 (cont.)

8. The **postpartum period is potentially dangerous. Patient** education for early detection **during and after pregnancy is** important.
9. Long-term health effects should be discussed.

New!

2013 Classification of Hypertensive Disorders of Pregnancy

- Four Categories
  1. Preeclampsia-eclampsia
  2. Chronic hypertension (of any cause)
  3. Chronic hypertension with superimposed preeclampsia
  4. Gestational hypertension

New!

Key Change:

Diagnosis of Preeclampsia:
Proteinuria Not Required

- Recognizes the syndromic nature of preeclampsia
- The disease affects all organ systems

1. Preeclampsia

WITHOUT* Severe Features** ***Versus ***WITH* Severe Features**

New!

Hypertension

Diagnostic Criteria for Preeclampsia	
	Definition
Blood Pressure	• Greater than or equal to 140 mm Hg systolic or greater than or equal to 90 mm Hg diastolic on two occasions at least 4 hours apart after 20 weeks of gestation in a woman with a previously normal blood pressure
Severe Hypertension	• Greater than or equal to 160 mm Hg systolic or greater than or equal to 110 mm Hg diastolic, hypertension can be confirmed within a short interval (minutes) to facilitate timely antihypertensive therapy

Created from: Task Force on Hypertension in Pregnancy. Executive Summary, 2013.

New!

Hypertension:

Systolic BP of 140 mmHg or higher, OR
Diastolic BP of 90 mmHg or higher

PLUS ONE of the following:	
Feature	**Definition**
• Proteinuria	≥300 mg protein/24 urine collection*, or a protein/creatinine ratio of ≥0.3 (each measured by mg/dL) **collection may be extrapolated from timed tests;*
• Thrombocytopenia	Platelets <100,000/microliter
• Impaired liver function	Increased serum liver transaminases to twice normal values
• New development of renal insufficiency	Elevated serum creatinine greater than 1.1 mg/dL, or a doubling of serum creatinine in the absence of other renal disease
• Pulmonary edema	
• New-onset cerebral or visual disturbances	

Created from: Task Force on Hypertension in Pregnancy. Executive Summary, 2013.

Preeclampsia

Hypertension* + **Evidence of Organ System Involvement**

- Systolic ≥140 mmHg
  Or
- Diastolic ≥90 mmHg

- Proteinuria
- Thrombocytopenia
- Impaired liver function
- New development of renal insufficiency
- Pulmonary edema
- New-onset cerebral or visual disturbances

*On two occasions at least 4 hours apart (in prev healthy pt after 20 wks)

Severe Features of Preeclampsia

ANY of these Findings	
Severe Feature	**Definition**
• Hypertension	• Systolic BP of 160 mmHg or higher, or • Diastolic BP of 110 mmHg or higher, on 2 occasions at least 4 hours apart while the patient is on bedrest (unless antihypertensive therapy is initiated before this time)
• Thrombocytopenia	Platelets <100,000/microliter
• Impaired liver function	Abnormally elevated blood concentrations of liver enzymes (to twice normal concentration), severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnoses, or both
• Progressive renal insufficiency	Serum creatinine concentration greater than 1.1 mg/dL or a doubling of serum creatinine concentration in the absence of other renal disease
• Pulmonary edema	
• New-onset cerebral or visual disturbances	

Created from: Task Force on Hypertension in Pregnancy. Executive Summary. 2013.

Preeclampsia

Hypertension* + **Evidence of Organ System Involvement**

- Systolic ≥140 mmHg
  Or
- Diastolic ≥90 mmHg

- Proteinuria
- Thrombocytopenia
- Impaired liver function
- New development of renal insufficiency
- Pulmonary edema
- New-onset cerebral or visual disturbances

*On two occasions at least 4 hours apart (in prev healthy pt after 20 wks)

Severe Preeclampsia

Hypertension* + **Evidence of Organ System Involvement**

- Systolic ≥140 mmHg
  Or
- Diastolic ≥90 mmHg

- Proteinuria
- Thrombocytopenia
- Impaired liver function
- New development of renal insufficiency
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Severe Features of Preeclampsia

Hypertension* + **Evidence of Organ System Involvement**

- Systolic ≥140 mmHg
  Or
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- Proteinuria
- Thrombocytopenia
- Impaired liver function
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*On two occasions at least 4 hours apart (in prev healthy pt after 20 wks)

Severe Features of Preeclampsia

Hypertension* + **Evidence of Organ System Involvement**

- **Systolic ≥160 mmHg**
  Or
- **Diastolic ≥110 mmHg**

- Proteinuria
- Thrombocytopenia
- Impaired liver function
- Renal insufficiency
- Pulmonary edema
- Cerebral or visual disturbances

*On two occasions at least 4 hours apart (in prev healthy pt after 20 wks)

New! 2013 Classification of Hypertensive Disorders of Pregnancy (cont.)

2. ***Chronic***: Hypertension that predates pregnancy
3. ***Gestational***: Hypertension is BP elevation after 20 weeks of gestation in the absence of proteinuria or the aforementioned systemic findings.
4. ***Superimposed Preeclampsia***: Chronic hypertension in association with preeclampsia.

New! Risk Factors for Preeclampsia

- Primiparity
- Prior preeclamptic pregnancy
- Chronic hypertension *or* chronic renal disease *or* both
- History of thrombophilia
- Multifetal pregnancy
- In vitro fertilization
- Family history of preeclampsia
- Type 1 or 2 diabetes mellitus
- Obesity
- Systemic lupus erythematosus
- Advanced maternal age (older than 40 years)

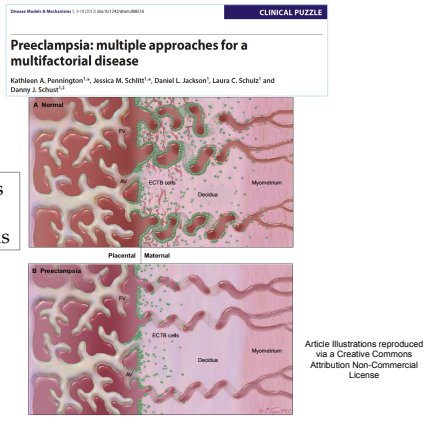
New! Key Observations

- ↑ Risk for Preeclampsia
  - ➢ Twofold to fourfold if the pt has a first-degree relative with a medical Hx of preeclampsia
  - ➢ Sevenfold if pt had preeclampsia in prior pregnancy
- Triplet Gestation Greater Risk than Twin; twin greater than singleton pregnancy

New! Prediction

- Current attempts have only produced modest prediction value (risk factors)
- No improvement in maternal or fetal outcome related to Uterine Artery Doppler screening (no randomized control trials)
  - ➢ may be technique/standardization issues
- Biomarkers for prediction said to be "integral" to disease stratification, targeted therapy

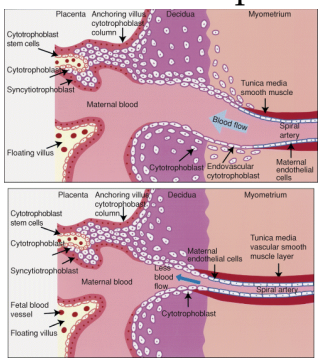
Biomarkers for angiogenesis



New! Angiogenesis-Related Biomarkers

- Several circulating anti-angiogenic proteins and pro-angiogenic proteins have been studied as possible biomarkers for preeclampsia
- Maternal risk factors + Biomarkers = show future promise as algorithms for predicting the disease
- However, the Task Force does **not** recommend using in clinical practice (no evidence that early screening improves outcomes)

Placental Implantation



Obstet Gynecol Sci. 2013 Jan;56(1):2-7. http://dx.doi.org/10.5468/OGS.2013.56.1.2

New Definition of Preeclampsia

- Based on research findings from past 10 years
- Emphasis on identification of preeclampsia based on the presence of hypertension and evidence of organ system involvement from any of the systems most susceptible to specific insults

Preeclampsia

- Current model of preeclampsia is one of **vascular mal-adaptations** stemming from implantation
- Results in **vessel epithelium injury** which may cause release of pro-inflammatory agents/mediators that produce cytokine release
- **Cytokines**, if released in large quantities, can produce the *Cytokine Release Syndrome* seen in some oncology patients when receiving chemotherapy using monoclonal antibodies.

Cytokines

- When cytokines are released into the circulation, systemic symptoms such as fever, nausea, chills, hypotension, tachycardia, asthenia, headache, rash, scratchy throat, and dyspnea can result.
- Abnormal vessel damage occurring in preeclampsia may have similar effects on pregnant patients, and lead to some of the signs of symptoms associated with HELLP syndrome.

Preeclampsia: Inflammatory Consequences

- Vessel damage may trigger complex inflammatory changes to the arterial endothelial layer, resulting in
  - Third spacing of fluid in pulmonary system (non-cardiogenic pulmonary edema)
  - Leftward shift in the oxyhemoglobin dissociation curve
  - Potential decreased oxygen consumption
  - Activation of the coagulation cascade, stimulation of pro- and anti-coagulants, and fibrinolysis

Diagnosis

- Hypertension

PLUS…

- Evidence of organ system involvement
  - Measure function of systems sensitive to hypoxemia, endothelial damage, reduced blood flow/O2 transport, etc.

Systemic Involvement

↓

Unpredictable Patterns of Cellular/ Organ System Stress and Injury

↓

Diagnosis Challenge

↓

Preeclampsia or Something Else?

Differential Diagnoses

	Preeclampsia	HELLP	Hepatitis	AFLP	ITP	HUS
Blood Pressure	Increased	Variable, or increased	WNL	Variable	WNL	WNL
Proteinuria	Increased	Variable, or increased	WNL	Variable	WNL	Increased
Hgb/Hct	Decreased	Decreased	Variable, decreased in sepsis	-	-	WNL
Platelets	WNL, decreased	Decreased	WNL	-	Decreased	WNL
Clotting factors	WNL, decreased	WNL, or decreased	Decreased	Decreased	WNL	WNL
Liver enzymes	WNL	Increased	Increased	Increased	WNL	WNL
Serum Glucose	WNL	WNL	WNL	Decreased	WNL	WNL
Creatinine	WNL, or increased	WNL, or increased	WNL, or increased	WNL, or increased	WNL	WNL, increased
Nausea & Vomiting	Some	Common	Common	Vomiting, nausea, gaging (very common)	-	-

TIME
Health & Family

PREGNANCY

Why Are More Pregnant Women Suffering Stroke?

By Tara Thean | Aug. 01, 2011 | Add a Comment

The rate of stroke is rising in pregnant women and in women who have just given birth, according to new research by the Centers for Disease Control and Prevention.

Between 1994-95 and 2006-07, the percentage of expectant women who were hospitalized for stroke rose 47%, while the percentage of new mothers who suffered stroke in the three months after delivery increased 83%. The total number of hospitalizations for stroke increased 54% over that decade.

MARTINE MOUCHY / GETTY IMAGES

"It's a little alarming," says lead study author Elena Kuklina. "It reminds us we should strive to take good care [of ourselves] before and during pregnancy."

The absolute number of strokes was still small, however, at 0.22 occurrences of stroke (up from 0.15) per 1,000 deliveries. Kuklina notes that stroke is a rare condition for women, but cautions that the findings suggest a particular risk among the study's population. "[The results] still tell us stroke is getting kind of younger, and pregnant women are especially at risk," she says.

Stroke in Pregnancy

- Incidence:
  - approximately 9 to 34 per 100,000
- Types
  - Intracerebral hemorrhage during pregnancy carries the highest morbidity and mortality, with an in-hospital mortality of 20%.

Stroke Causes

Unique to *Pregnancy*	Non-Pregnant Women
• Preeclampsia/eclampsia • Postpartum angiopathy • Amniotic fluid embolism • Postpartum Cardiomyopathy	• Hypertension • Diabetes • Vasculitis • Arteriovenous malformations • Aneurysms

Tate, J. Pregnancy and stroke risk in women. *Women's Health*. 2011 May; 7(3):363-74.

Stroke in Pregnancy: Risk Factors

- Hyperemesis gravidarum
- Anemia
- Thrombocytopenia
- Postpartum hemorrhage
- Transfusion
- Fluid, electrolyte and acid-base disorders
- Infection

- >35 years
- African–American
- Preeclampsia/eclampsia/ gestational hypertension
- Thrombophilias
- Migraine headaches
- Diabetes
- Chronic hypertension

Key Clinical Pearl

Controlling blood pressure is the optimal intervention to prevent deaths due to stroke in women with preeclampsia.

Over the last decade, the UK has focused QI efforts on aggressive treatment of both systolic and diastolic blood pressure and has demonstrated a reduction in deaths.

Case Study PEMD.05

Question?

What is the lowest value of systolic blood pressure that would classify a patient as having "**severe**" preeclampsia?

A. Systolic ≥ 180 mmHg
B. Systolic ≥ 160 mmHg
C. Systolic ≥ 140 mmHg
D. Systolic ≥ 120 mmHg

Case Study PEMD.05

Question?

What is the lowest value of systolic blood pressure that would classify a patient as having "**severe**" preeclampsia?

A. Systolic > 180 mmHg
B. Systolic ≥ 160 mmHg
C. Systolic ≥ 140 mmHg
D. Systolic ≥ 120 mmHg

ACOG Hypertensive Emergency Treatment Guidelines, CO #514

2011

The American College of Obstetricians and Gynecologists
Woman's Health Care Physicians

COMMITTEE OPINION

Number 514 • December 2011

Committee on Obstetric Practice

This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

Emergent Therapy for Acute-Onset, Severe Hypertension With Preeclampsia or Eclampsia

ABSTRACT: Acute-onset, persistent (lasting 15 minutes or more), severe systolic (greater than or equal to 160 mm Hg) or severe diastolic hypertension (greater than or equal to 110 mm Hg) or both in pregnant or postpartum women with preeclampsia or eclampsia constitutes a hypertensive emergency. Severe systolic hypertension may be the most important predictor of cerebral hemorrhage and infarction in these patients and if not treated expeditiously can result in maternal death. Intravenous labetalol and hydralazine are both considered first-line drugs for the management of acute, severe hypertension in this clinical setting. Close maternal and fetal monitoring by the physician and nursing staff are advised. Order sets for the use of labetalol and hydralazine for the initial management of acute, severe hypertension in pregnant or postpartum women with preeclampsia or eclampsia have been developed.

Even Newer 2015! ACOG 2015

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

COMMITTEE OPINION

Number 623 • February 2015 *(Replaces Committee Opinion Number 514, December 2011)*

Committee on Obstetric Practice

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Emergent Therapy for Acute-Onset, Severe Hypertension During Pregnancy and the Postpartum Period

"Hypertensive Emergency"

- Acute-onset
- Severe Hypertension
  - Systolic ≥160 mm Hg, **OR**
  - Diastolic ≥110 mm Hg,
  - OR Both
- Accurately measured using standard techniques and
- Persistent for ≥15 minutes [is considered] a **hypertensive emergency**.

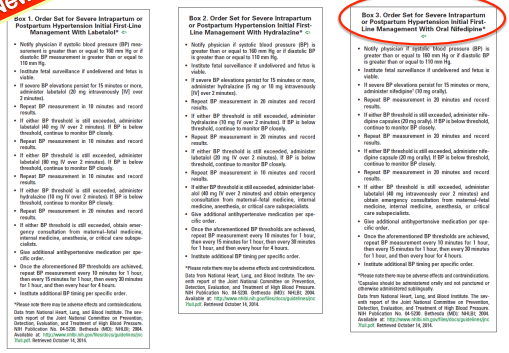
Emergent therapy for acute-onset, severe hypertension with pre- eclampsia or eclampsia. Committee Opinion No. 514. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;118: 1465–8

Link to:
ACOG Committee Opinion:
2015 ACOG Emergent Therapy for Acute-Onset, Severe Hypertension During Pregnancy and the Postpartum Period

http://www.acog.org/Resources-And-Publications/Committee-Opinions/Committee-on-Obstetric-Practice/Emergent-Therapy-for-Acute-Onset-Severe-Hypertension-During-Pregnancy-and-the-Postpartum-Period

Newer 2015!

ACOG, 2015 HYTN



Box 1. Order Set for Severe Intrapartum or Postpartum Hypertension Initial First-Line Management With Labetalol*

- Notify physician if systolic blood pressure (BP) remains greater than or equal to 160 mm Hg or if diastolic BP measurement is greater than or equal to 110 mm Hg.
- Institute fetal surveillance if undelivered and fetus is viable.
- If severe BP elevations persist for 15 minutes or more, administer labetalol (20 mg intravenously [IV] over 2 minutes).
- Repeat BP measurement in 10 minutes and record results.
- If either BP threshold is still exceeded, administer labetalol (40 mg IV over 2 minutes). If BP is below threshold, continue to monitor BP closely.
- Repeat BP measurement in 10 minutes and record results.
- If either BP threshold is still exceeded, administer labetalol (80 mg IV over 2 minutes). If BP is below threshold, continue to monitor BP closely.
- Repeat BP measurement in 10 minutes and record results.
- If either BP threshold is still exceeded, administer hydralazine (10 mg IV over 2 minutes). If BP is below threshold, continue to monitor BP closely.
- Repeat BP measurement in 20 minutes and record results.
- If either BP threshold is still exceeded, obtain emergency consultation from maternal–fetal medicine, internal medicine, anesthesia, or critical care subspecialists.
- Give additional antihypertensive medication per specific order.
- Once the aforementioned BP thresholds are achieved, repeat BP measurement every 15 minutes for 1 hour, then every 15 minutes for 1 hour, then every 30 minutes for 1 hour, and then every hour for 4 hours.
- Institute additional BP timing per specific order.

*Please note there may be adverse effects and contraindications.

Data from National Heart, Lung, and Blood Institute. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. NIH Publication No. 04-5230. Bethesda (MD): NHLBI; 2004. Available at: http://www.nhlbi.nih.gov/files/docs/guidelines/jnc7full.pdf. Retrieved October 14, 2014.

Box 2. Order Set for Severe Intrapartum or Postpartum Hypertension Initial First-Line Management With Hydralazine*

- Notify physician if systolic blood pressure (BP) is greater than or equal to 160 mm Hg or if diastolic BP is greater than or equal to 110 mm Hg.
- Institute fetal surveillance if undelivered and fetus is viable.
- If severe BP elevations persist for 15 minutes or more, administer hydralazine (5 mg or 10 mg intravenously [IV] over 2 minutes).
- Repeat BP measurement in 20 minutes and record results.
- If either BP threshold is still exceeded, administer hydralazine (10 mg IV over 2 minutes). If BP is below threshold, continue to monitor BP closely.
- Repeat BP measurement in 20 minutes and record results.
- If either BP threshold is still exceeded, administer labetalol (20 mg IV over 2 minutes). If BP is below threshold, continue to monitor BP closely.
- Repeat BP measurement in 10 minutes and record results.
- If either BP threshold is still exceeded, administer labetalol (40 mg IV over 2 minutes) and obtain emergency consultation from maternal–fetal medicine, internal medicine, anesthesia, or critical care subspecialists.
- Give additional antihypertensive medication per specific order.
- Once the aforementioned BP thresholds are achieved, repeat BP measurement every 10 minutes for 1 hour, then every 15 minutes for 1 hour, then every 30 minutes for 1 hour, and then every hour for 4 hours.

*Please note there may be adverse effects and contraindications.

Data from National Heart, Lung, and Blood Institute. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. NIH Publication No. 04-5230. Bethesda (MD): NHLBI; 2004. Available at: http://www.nhlbi.nih.gov/files/docs/guidelines/jnc7full.pdf. Retrieved October 14, 2014.

Box 3. Order Set for Severe Intrapartum or Postpartum Hypertension Initial First-Line Management With Oral Nifedipine*

- Notify physician if systolic blood pressure (BP) is greater than or equal to 160 mm Hg or if diastolic BP is greater than or equal to 110 mm Hg.
- Institute fetal surveillance if undelivered and fetus is viable.
- If severe BP elevations persist for 15 minutes or more, administer nifedipine† (10 mg orally).
- Repeat BP measurement in 20 minutes and record results.
- If either BP threshold is still exceeded, administer nifedipine capsules (20 mg orally). If BP is below threshold, continue to monitor BP closely.
- Repeat BP measurement in 20 minutes and record results.
- If either BP threshold is still exceeded, administer nifedipine capsule (20 mg orally). If BP is below threshold, continue to monitor BP closely.
- Repeat BP measurement in 20 minutes and record results.
- If either BP threshold is still exceeded, administer labetalol (40 mg intravenously over 2 minutes) and obtain emergency consultation from maternal–fetal medicine, internal medicine, anesthesia, or critical care subspecialists.
- Give additional antihypertensive medication per specific order.
- Once the aforementioned BP thresholds are achieved, repeat BP measurement every 10 minutes for 1 hour, then every 15 minutes for 1 hour, then every 30 minutes for 1 hour, and then every hour for 4 hours.
- Institute additional BP timing per specific order.

*Please note there may be adverse effects and contraindications.

†Nifedipine should be administered orally and not punctured or sublingually to avoid precipitous hypotension.

Data from National Heart, Lung, and Blood Institute. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. NIH Publication No. 04-5230. Bethesda (MD): NHLBI; 2004. Available at: http://www.nhlbi.nih.gov/files/docs/guidelines/jnc7full.pdf. Retrieved October 14, 2014.

ACOG, 2015 HYTN: Box 3
Oral Nifedipine as First Line Agent

New in 2015!

- Notify physician if systolic blood pressure (BP) is greater than or equal to 160 mm Hg or if diastolic BP is greater than or equal to 110 mm Hg.
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- If either BP threshold is still exceeded, administer nifedipine capsule (20 mg orally). If BP is below threshold, continue to monitor BP closely.
- Repeat BP measurement in 20 minutes and record results.
- If either BP threshold is still exceeded, administer labetalol (40 mg intravenously over 2 minutes) and obtain emergency consultation from maternal–fetal medicine, internal medicine, anesthesia, or critical care subspecialists.
- Give additional antihypertensive medication per specific order.
- Once the aforementioned BP thresholds are achieved, repeat BP measurement every 10 minutes for 1 hour, then every 15 minutes for 1 hour, then every 30 minutes for 1 hour, and then every hour for 4 hours.
- Institute additional BP timing per specific order.

Publically accessible at www.acog.org

Physiology of Blood Pressure

Blood Pressure = Flow x Resistance

MAP= Cardiac Output (CO) **X** Systemic Vascular Resistance (SVR)

Antique Fire Hose Nozzles

BP = Flow x Resistance

- Antihypertensive agents will typically reduce "flow" (cardiac output), **OR** "resistance" (SVR), or both.
- Some side effects are therefore, consequences of too much reduction in cardiac output or SVR.

Antihypertensive Medications in Preeclampsia

"Round up the usual suspects"

1st Line Antihypertensive Meds
- Hydralazine
- Labetalol
- Nifedipine

2nd Line Antihypertensive Meds
- Nicardipine
- Others

3rd Line (FINAL) Antihypertensive Med
- Sodium nitroprusside

Antihypertensive Meds

- There is no evidence that pharmacological treatment improves neonatal outcomes in women with mild hypertension.
- However, treatment-induced reduction in mean arterial pressure may increase the frequency of small for gestational age (SGA) infants.
- "In all cases, treatment should be re-instituted once BP reaches 150–160 mmHg systolic or 100–110 mmHg diastolic, in order to prevent increases in BP to very high levels during pregnancy."

http://www.perinatology.com/Reference/OBPharmacopoeia-Public/Antihypertensives.htm

ACOG 2011

The American College of Obstetricians and Gynecologists
Women's Health Care Physicians
COMMITTEE OPINION
Number 514 • December 2011
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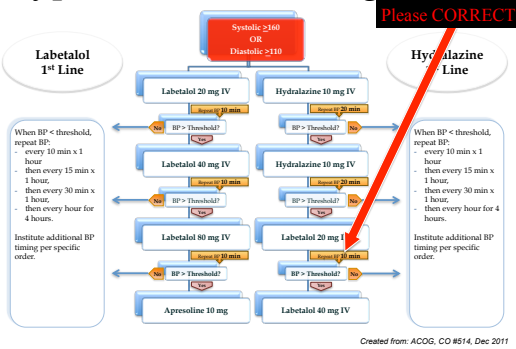
Emergent Therapy for Acute-Onset, Severe Hypertension With Preeclampsia or Eclampsia

- Intravenous labetalol and hydralazine* are both considered first-line drugs for the management of acute, severe hypertension in this clinical setting.
- Close maternal and fetal monitoring by the physician and nursing staff are advised.
- Order sets for the use of labetalol and hydralazine for the initial management of acute, severe hypertension in pregnant or postpartum women with preeclampsia or eclampsia have been developed.

Hypertensive Crisis Algorithm

Please CORRECT!



Created from: ACOG, CO #514, Dec 2011

New 2011

Order Set for Severe Intrapartum or Postpartum Hypertension Initial First-Line Management with Labetalol*

"Box 1"

1. Notify physician if systolic ≥ 160 mm Hg or if diastolic ≥ 110 mm Hg.
2. Institute fetal surveillance if undelivered and fetus is viable.
3. Administer labetalol (20 mg IV over 2 minutes).
4. Repeat BP measurement in 10 minutes; record results.
5. If either BP > threshold, administer labetalol (40 mg IV over 2 minutes). If BP is below threshold, continue to monitor BP closely.
6. Repeat BP measurement in 10 minutes and record results.
7. If either BP > threshold is, administer labetalol (80 mg IV over 2 minutes). If BP is below threshold, continue to monitor BP closely.
8. Repeat BP measurement in 10 minutes and record results.
9. If either BP > threshold, administer hydralazine (10 mg IV over 2 minutes). If BP is below threshold, continue to monitor BP closely.
10. Repeat BP measurement in 20 minutes and record results.
11. If either BP > threshold, obtain emergency consultation from MFM, IM, anesthesia, or critical care specialists.
12. Give additional antihypertensive medication per specific order (Nicardipine).
13. Once the aforementioned BP thresholds are achieved, repeat BP measurement every 10 minutes for 1 hour, then every 15 minutes for 1 hour, then every 30 minutes for 1 hour, and then every hour for 4 hours.
14. Institute additional BP timing per specific order.

Emergent therapy for acute-onset, severe hypertension with pre-eclampsia or eclampsia. Committee Opinion No. 514. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;118: 1465–8

New 2011

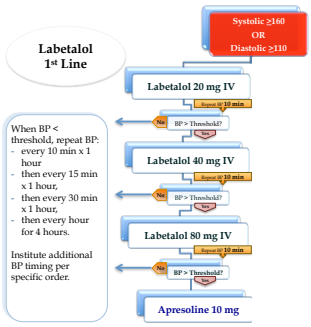
Physician Order Set for
Severe Intrapartum or Postpartum Hypertension
Initial First-Line Management with LABETALOL

Antihypertensive Therapy with LABETALOL HYDROCHLORIDE in Preeclampsia-Eclampsia

1. Notify physician if systolic blood pressure is greater than or equal to (≥) 160 mmHg, or if diastolic blood pressure is greater than or equal to (≥) 110 mmHg.
2. Fetal surveillance if mother antepartum and fetus viable. [See unit guidelines for fetal assessment modality based on gestational age.]
3. Administer labetalol hydrochloride (HCL) 20 milligrams intravenously over two (2) minutes.
4. Repeat Blood Pressure (BP) measurement in 10 minutes.
5. If either systolic or diastolic BP greater than threshold, administer labetalol HCL 40 milligrams intravenously over two (2) minutes. If BP is below threshold, continue to monitor BP closely.
6. Repeat BP measurement in ten (10) minutes and record results.
7. If either systolic or diastolic BP is greater than threshold, administer labetalol HCL 80 mg intravenously over two (2) minutes. If BP is below (less than) threshold, continue to monitor BP closely.
8. Repeat BP measurement in ten (10) minutes.
9. If either systolic or diastolic BP is greater than threshold, administer hydralazine 10 mg IV over two (2) minutes. If BP is below threshold, continue to monitor BP closely.
10. Repeat BP measurement in twenty (20) minutes and record results.
11. If either systolic or diastolic BP greater than threshold, obtain emergency consultation from MFM, IM, anesthesia, or critical care specialist(s).
12. Give additional antihypertensive medication per specific order.
13. Once the aforementioned BP thresholds are achieved, repeat BP measurement every ten (10) minutes for one (1) hour, then every fifteen (15) minutes for one (1) hour, then every thirty (30) minutes for one (1) hour, and then every hour for four (4) hours.
14. Institute additional BP timing per specific order.

Physician/Provider Name _____ Signature _____ Date _____ Time _____

Hypertensive Crisis Algorithm



Created from: ACOG, CO #514, Dec 2011

New 2011

Order Set for Severe IP or PP Hypertension
Initial First-Line Management with Hydralazine*

"Box 2"

1. Notify physician if systolic BP is greater than or equal to 160 mm Hg or if diastolic BP is greater than or equal to 110 mm Hg.
2. Institute fetal surveillance if undelivered and fetus is viable.
3. Administer hydralazine (5 mg or 10 mg IV over 2 minutes).
4. Repeat BP measurement in 20 minutes and record results.
5. If either BP threshold is still exceeded, administer hydralazine (10 mg IV over 2 minutes). If BP is below threshold, continue to monitor BP closely.
6. Repeat BP measurement in 20 minutes and record results.
7. If either BP threshold is still exceeded, administer labetalol (20 mg IV over 2 minutes). If BP is below threshold, continue to monitor BP closely.
8. Repeat BP measurement in 10 minutes and record results.
9. If either BP threshold is still exceeded, administer labetalol (40 mg IV over 2 minutes) and obtain emergency consultation from MFM, IM, anesthesia, or critical care specialists.
10. Give additional antihypertensive medication per specific order.
11. Once the aforementioned BP thresholds are achieved, repeat BP measurement every 10 minutes for 1 hour, then every 15 minutes for 1 hour, then every 30 minutes for 1 hour, and then every hour for 4 hours.
12. Institute additional BP timing per specific order.

Emergent therapy for acute-onset, severe hypertension with pre-eclampsia or eclampsia. Committee Opinion No. 514. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;118: 1465-8

New 2011

Physician Order Set for
Severe Intrapartum or Postpartum Hypertension
Initial First-Line Management with HYDRALAZINE

Antihypertensive Therapy with HYDRALAZINE in Preeclampsia-Eclampsia

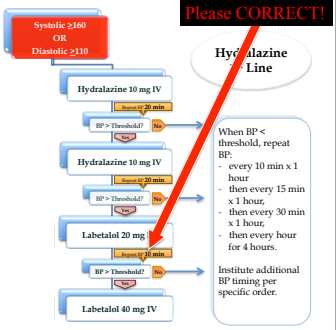
1. Notify physician if systolic blood pressure (BP) is greater than or equal to (≥) 160 mmHg, or if diastolic BP is greater than or equal to (≥) 110 mmHg.
2. Fetal surveillance if mother antepartum and fetus viable. [See unit Guidelines for fetal assessment modality based on gestational age.]
3. Administer hydralazine 5 milligrams or 10 milligrams intravenously over two (2) minutes.
4. Repeat BP measurement in twenty (20) minutes.
5. If either BP threshold is still exceeded, administer hydralazine 10 milligrams intravenously over two (2) minutes). If BP is below threshold, continue to monitor BP closely.
6. Repeat BP measurement in twenty (20) minutes.
7. If either BP threshold is still exceeded, administer labetalol 20 milligrams Intravenously over two (2) minutes. If BP is below threshold, continue to monitor BP closely.
8. Repeat BP measurement in ten (10) minutes.
9. If either BP threshold is still exceeded, administer labetalol 40 milligrams intravenously over two (2) minutes and obtain emergency consultation from MFM, IM, anesthesia, or critical care specialists.
10. Give additional antihypertensive medication per specific order.
11. Once the aforementioned BP thresholds are achieved, repeat BP measurement every ten (10) minutes for one (1) hour, then every fifteen (15) minutes for one (1) hour, then every thirty (30) minutes for one (1) hour, and then every hour for four (4) hours.
12. Institute additional BP timing per specific order.

Physician/Provider Name _____ Signature _____ Date _____ Time _____

Abbreviations: > = greater than or equal to, mmHg = millimeters of mercury, MFM = Maternal Fetal Medicine, IM = Internal Medicine

Hypertensive Crisis Algorithm

Please CORRECT!



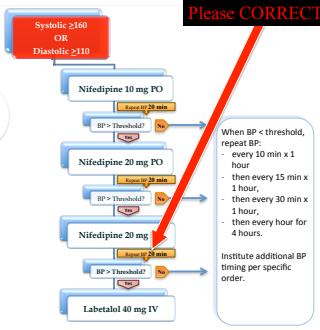
Created from: ACOG, CO #514, Dec 2011

Hypertensive Crisis Algorithm

Newer 2015!

Please CORRECT!

ORAL
Nifedipine
1st Line



Created from: ACOG, CO #623, Feb 2015

Hypertensive Medication Administration: Oral versus IV

- First line therapy recommendations for acute treatment of critically elevated BP in pregnant women (160/105-110) are either IV labetalol or IV hydralazine.
- If acute treatment needed in a patient without IV - oral nifedipine may be used (10 mg) and may be repeated in 30 minutes.
- PO (oral) nifedipine appears equally as efficacious as IV labetalol in correcting severe BP elevations.
- Oral labetalol would be expected to be less effective in acutely lowering the BP due to a slower onset to peak action; should be used only if oral nifedipine is not available in a patient without IV access.

ACOG Practice Bulletin #33, Reaffirmed 2012; ACOG Committee Opinion #514, 2012; Tuffnell D, Jankowitcz D, Lindow S, et al. BJOG 2005;112:875-880.

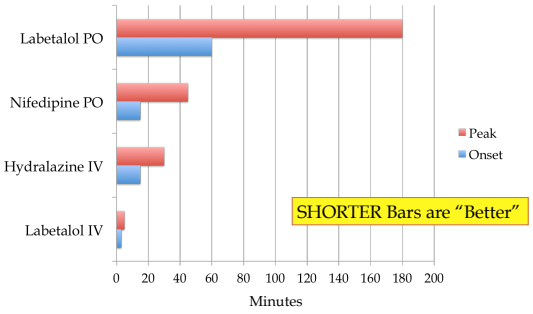
Hypertensive Medication Administration: Oral versus IV

- IV Labetalol
  - Onset: 2-5 min
  - Peak: 5 min
- PO Labetalol:
  - Onset: 20 min-2 hrs
  - Peak: 1-4 hrs
- IV Hydralazine
  - Onset: 5-20 min
  - Peak: 15-30 min
- PO Nifedipine
  - Onset: 5-20 min*
  - Peak: 30-60 min

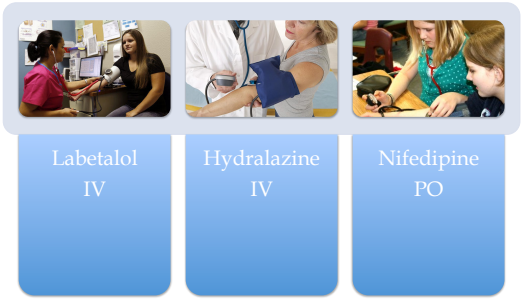
Raheem I, Saiid R, Omar S, et al. Oral nifedipine versus intravenous labetalol for acute blood pressure control in hypertensive emergencies of pregnancy: a randomized trial. BJOG 2012;119:78-85.

http://www.uspharmacist.com/content/d/feature/i/1444/c/27112/
Current Cardiovascular Drugs, edited by William H. Frishman, Angela Cheng-Lai, James Nawarskas, 4th edition 2005 pg. 2-186 51

Hypertensive Medication Administration: Oral versus IV



"First Line" Therapy

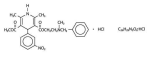


"2nd Line" Therapy

- Alternatives to consider:
  - Continuous intravenous infusion (pump) of Labetalol or Nicardipine
    - Minimal transplacental passage and changes in umbilical artery Doppler velocimetry have been noted

Emergent therapy for acute-onset, severe hypertension with pre-eclampsia or eclampsia. Committee Opinion No. 514. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;118: 1465-8

Nicardipine HCL



- Is a calcium ion influx inhibitor (slow channel blocker or calcium channel blocker).
- Produces significant decreases in systemic vascular resistance.
- Indicated for the short-term treatment of hypertension when oral therapy is not feasible or not desirable.
- Metabolized extensively by the liver - plasma concentrations are influenced by changes in hepatic function
- Contraindicated in patients with advanced aortic stenosis because of the reduced afterload. Reduction of diastolic pressure in these patients may worsen rather than improve myocardial oxygen balance.
- Pregnancy Category C

Nicardipine:
Rapid Onset and Peak Action

Drug	Half Life (time)
Labetalol	5.5 hours
Hydralazine	4 hours
Nicardipine*	**2 to 5 minutes**
Nifedipine	2 to 5 hours

*Contraindications to the use of nicardipine are hypersensitivity to nicardipine, severe aortic stenosis, hypotension, and shock.

Nij Bijvank, SW (2010). Nicardipine for treatment of severe hypertension in pregnancy. ObGyn Sur 65,5:341-7.

Starting Dose and Titration

- Non-pregnant patient:
  - Starting dose 3 to 5 mg/hour
  - Increase rate by 2.5 mg/hour every 5 minutes to a maximum of 15 mg/hour
- ***Pregnancy***
  - Starting dose 1 to 3 mg/hour
  - Increase by 0.5 to 1.0 mg/hour to maximum of 10 mg/hour until the target BP is reached

Nij Bijvank, SW (2010). Nicardipine for treatment of severe hypertension in pregnancy. ObGyn Sur 65,5:341-7.

Maternal and Fetal/Neo Adverse Effects of Intravenous Nicardipine in 147 Patients

Maternal	
Transient hypotension	8
Nausea	3
Palpitations	3
Headache	11
Flushing	8

Fetal/Neonatal	
Bradycardia	0
Decelerations	2
Loss of variability	1
Preterm delivery	59
Small for gestational age	24
Apgar score <7 after 5 mins	3

Nij Bijvank, SW (2010). Nicardipine for treatment of severe hypertension in pregnancy. ObGyn Sur 65,5:341-7.

Non-Responders:
Sodium Nitroprusside (Nipride®)

"When Nothing Works . . ."

- Sodium nitroprusside should be reserved for extreme emergencies and used for the shortest amount of time possible.
- Rationale/side effects:
  - Cyanide and thiocyanate toxicity in the mother *and* fetus or newborn *(monitor maternal levels during administration)*
  - Increased intracranial pressure with potential worsening of cerebral edema in the mother.

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HIGH RISK & CRITICAL CARE OB
A Forensic Case Studies Approach

Day One	8:00 AM to 4:00 PM
Background:	Distressing facts and stats on maternal deaths
Case Study:	"AP patient with severe hypotension unresponsive to fluid bolus" •Are you able to identify SHOCK? •Volume resuscitation quick "Rules" for treatment
Case Study:	**"Post C-section patient with preeclampsia & new onset complaints of 'tight chest' and difficulty breathing"** •Hypertension disorders •The hemodynamic spectrum of preeclampsia •Early recognition of pulmonary edema •*PRE v. HELLP v. Infectious Hepatitis v. HUS v. TTP v. AFLP*
Case Study:	"Preterm patient with grand mal seizures en route to hospital" •Magnesium Sulfate: "High Alert Status" •Magnesium Sulfate Myths vs. Science
Case Study *(cont)*:	"IP patient with severe preeclampsia and hypertensive urgency" •ACOG's opinion on antihypertensive(s) treatment: New Algorithms •Nicardipine (Old drug: New Options) •What to give when first-line agents fail

Post C-section patient with preeclampsia & new onset complaints of 'tight chest' and difficulty breathing

Post C/S fetal intolerance to labor

- L&D Recovery Room
- 27 year old, G_1P_1 delivered of a 33 $^{2/7}$ weeks gestation, Dx: preeclampsia
- Cervidil, oxytocin induction
- EFM: Category I & II; persistent Category II with loss of accelerations; increasing FHR baseline
- Induction maternal blood pressures (BP): 145/88, 150/92, 142/80, 144/92, 157/90, 160/90

Preeclampsia Post C/S

- Operating Room I&O
  - EBL: 800 mL

	IV	Meds	Blood	TOTAL
Intake	2400	100	0	2500 mL
	Urine	EBL	Emesis	TOTAL
Output	50	800	50	900 mL

L&D PACU – Page 1

Time	BP	HR	RR	Temp	SaO2	UOP	Notes
17:55	110/70	108	16	97.2/36.2	.98	emptied	
18:00	114/76	110	16		.99		
18:05	122/82	100			.98		
18:10	108/70	104	16		.97		
18:15	108/88	108			--		
18:20	102/76	99			--		
18:25	140/95	81	16		.98		
18:30	125/96	94			.96		
18:35	138/90	102			.97		
18:40	130/100	108			.97		
18:45	144/96	110	16		.98		

L&D PACU – Page 2

Time	BP	HR	RR	Temp	SaO2	UOP	Notes
19:00	145/93	110	18		.97	55 mL	
19:15	155/100	107			.96		
19:30	140/99	113			.95		
19:45	146/102	108			.97		
20:00	137/104	115	24		.95	30 mL	RR noted
20:15	144/104	122			.93		Anes bedside
20:20	128/90	119			.94		NC to FM
20:25	132/105	121	26		.93		
20:30	156/100	107			.93		
20:35	150/106	105			.94		
20:40	152/96	112			.92		

What is your differential diagnosis at this point?

Answer the following questions:

1. Why is the patient tachycardic?
2. Why is she tachypnic?
3. Why are her BP's increasing?
4. Why is her SpO2 decreasing?
5. What other information do you need to answer the questions?
   - Assessments
   - Labs
   - Studies

L&D PACU – Page 3

Back

Time	BP	HR	RR	Temp	SaO2	UOP	Notes
20:45	145/101	118			.94		
20:50	157/107	120	26		--		
20:55	150/90	120			.92		
21:00	146/102	108			.91	16 mL	Anes, OB, RT call 2 bs
21:05	146/96	116	30(?)		.91		ABG/ morphine
21:10	150/106	120			.90		
21:15	140/109	126	35	98.0/36.6	.89		
21:20	152/98	121			.90		
21:25	156/100	130			.89		
21:30		10			.91		
21:35	152/96	136			.88		

Preeclampsia Post C/S

Back

- Arterial Blood Gas (ABG)

ABG	Value	Nml 3rd trimester	Units
Time	21:07		
pH	7.34	7.39 – 7.45	
pCO_2	42	25 – 33	mmHg
pO_2	68	92 – 107	mmHg
HCO_3	17	16 – 22	mEq/L
SaO_2	89	98-100	Percent (%)

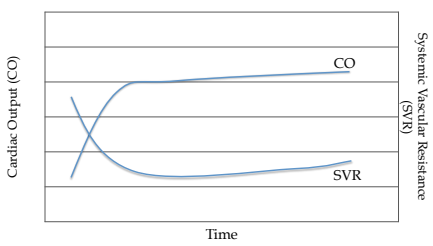
Problem List

- Hypertension
- Uncompensated respiratory acidosis; loss of buffering capability; impending metabolic acidosis…
- Pulmonary insufficiency, respiratory compromise
- ? Heart failure
- ? Pulmonary edema
- ? End organ system derangements

Preeclampsia: Hemodynamics

- One pathway for hemodynamic alterations specific to preeclampsia is thought to begin with or shortly after implantation.
- Complex signaling of the abnormal placental vascular sites may also trigger increased maternal cardiac output at significantly higher volumes compared with normal pregnancy.

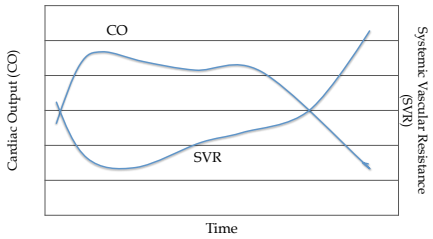
Hemodynamic Changes in Normal Pregnancy



Preeclampsia: Hemodynamics

- Early increase in CO results in a compensatory decreased in SVR, but likely exposes endothelial cells to sheering damage from flow.
- To compensate and protect end organs, the endothelial signal the arterial muscle cells to begin constricting to decrease sheering forces.
- Over time, the arterial constriction contributes to elevated SVR that ultimately decreases CO.

Hemodynamic Changes in Preeclampsia with High Output



Labs, Tests, Plan

- Auscultation of lungs (later sign)
- Chest x-ray (late sign)
- Renal function labs
- Chemistry
- CBC with differential
- Liver function labs
- Cardiac function (echo) and enzymes (R/O MI)

Urgent Actions

- Respiratory/pulmonary consult (stat)
- Bedside intubation and mechanical ventilation
- BP severely elevated at intubation -
- Pink, frothy sputum when tube placed
- Wide pulmonary shunt fraction
- Decreased left ventricular contractility

Treatment and Outcome

- Non-cardiogenic pulmonary edema secondary to preeclampsia
- Mechanical ventilation x 3.5 days
- Slightly elevated cardiac enzymes; peaking in 1st 24 hours of intubation/ cardiac failure
- Abnormal renal function – ATN; resolving prior to D/C on post partum day 11 (follow-up with nephrology)
- Echo WNL at D/C

Preeclampsia

- Abnormal vessels – stress
- Endothelial involvement
- Stimulation of inflammatory system – whole body
- Production of fibrin polymers, activation of fibrinolysis
- Perfusion challenges – mechanical/chemical/ electrical
- Cellular consequences
- Organ system involvement
- Impaired oxygen transports and utilization

Physiology of Blood Pressure

Blood Pressure = Flow x Resistance

MAP= Cardiac Output (CO) **X** Systemic Vascular Resistance (SVR)

MAP = CO x SVR

- Elevated BP may be caused by
  - Increased CO and normal to low normal SVR

    OR
  - Increased SVR and decreased CO

  QUESTION: How do you know which one your patient has?

Measure SVR

$$\textbf{SVR} = \frac{\textbf{MAP – CVP}}{\textbf{CO}} \textbf{ X 80}$$

Example: BP = 170/88

"High CO, normal to low-normal SVR"

- SAMPLE Pt #1
  - HR 100
  - RR 18
  - CVP 5 mmHg
  - PAP 26/10
  - PCOP 10
  - C.O. 8.7 L/minute
  - SVR - ???

"High SVR, low CO"

- SAMPLE Pt #2
  - HR 100
  - RR 18
  - CVP 5 mmHg
  - PAP 34/16
  - PCOP 16
  - C.O. 4.2 L/minute
  - SVR -???

SVR

"High CO, normal to low-normal SVR"

SVR = ?

- MAP = 115
- [(MAP-CVP)/CO] x 80
- =[(115-5)/8.7] x 80
- =[110/8.7] x 80
- = 12.6 x 80
- = 1012

SVR = 1012

"High SVR, low CO"

SVR = ?

- MAP = 115
- [(MAP-CVP)/CO] x 80
- =[(115-5)/4.2] x 80
- =[110/4.2] x 80
- = 26.2 x 80
- = 2095

SVR = 2095

What Type of Antihypertensive Drug Would Work BEST for Each Patient?

"High CO, normal to low-normal SVR"

SVR = ?

- MAP = 115
- [(MAP-CVP)/CO] x 80
- =[(115-5)/8.7] x 80
- =[110/8.7] x 80
- = 12.6 x 80
- = 1012

SVR = 1012

"High SVR, low CO"

SVR = ?

- MAP = 115
- [(MAP-CVP)/CO] x 80
- =[(115-5)/4.2] x 80
- =[110/4.2] x 80
- = 26.2 x 80
- = 2095

SVR = 2095

What Type of Antihypertensive Drug Would Work BEST for Each Patient?

"High CO, normal to low-normal SVR"

SVR = ?

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- [(MAP-CVP)/CO] x 80
- =[(115-5)/8.7] x 80
- =[110/8.7] x 80
- = 12.6 x 80
- = 1012

SVR = 1012

"High SVR, low CO"

SVR = ?

- MAP = 115
- [(MAP-CVP)/CO] x 80
- =[(115-5)/4.2] x 80
- =[110/4.2] x 80
- = 26.2 x 80
- = 2095

SVR = 2095

Labetalol v. Hydralazine?

Summary