



Caring for Two in the ICU: Managing Critical Illness in Pregnancy

Tuesday, December 6, 2016

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Disclosure

- The program chair and presenters for this continuing education activity have reported no relevant financial relationships, except:
- **Julie Kelsey** - Pfizer: Stockholder/Ownership Interest



Pulmonary Embolism During Pregnancy

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Objectives

- Appraise a pregnant woman's risk for thrombosis and evaluate diagnostic testing in pregnancy.
- Devise a treatment strategy for the management of pulmonary embolism in the critically ill pregnant patient.
- Design an anticoagulation plan for a women with a pulmonary embolism following acute therapy.

Thromboembolism in Pregnancy

- Most common cause of maternal death in developed countries
- 9% of all maternal deaths
- Incidence of PE in pregnancy in the U.S. is 200 per 100,000 woman years
 - Risk of VTE 4-5 fold higher than nonpregnant women
- Highest risk during the first week postpartum

Risk Factors for Pulmonary Embolism

- Age > 35
- History of thromboembolism
- Obesity
- Thrombophilia (hereditary or acquired)
- Smoking
- Significant varicose veins
- Prolonged travel or bedrest \geq 3 days
- Systemic infection (pyelonephritis, pneumonia, wound infection)

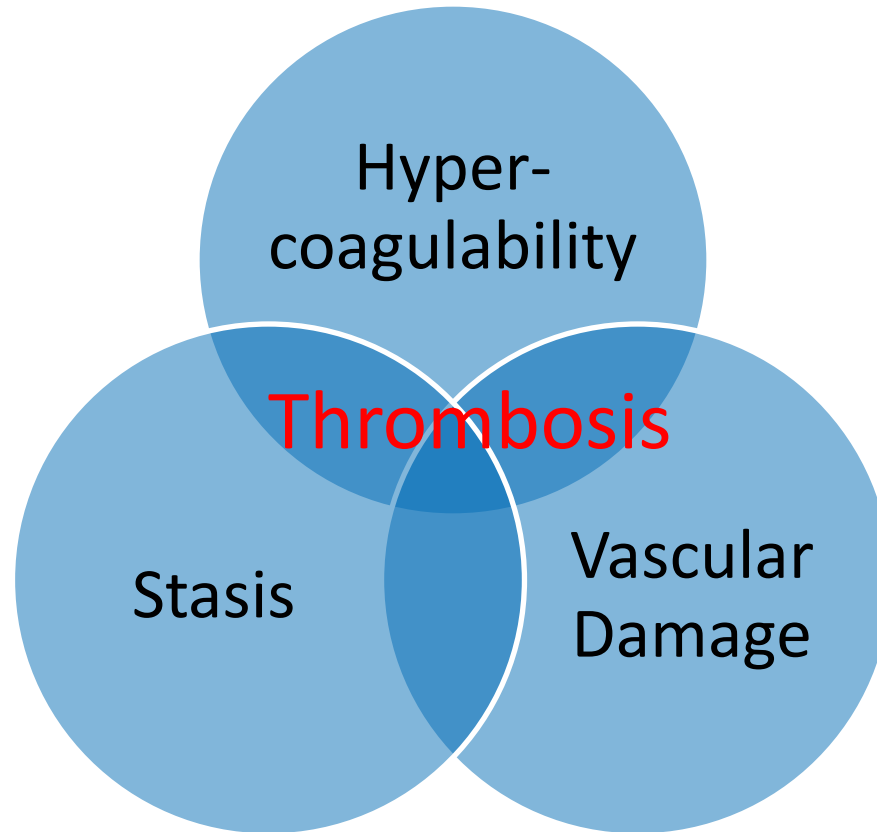
Risk Factors Specific to Pregnancy

- Parity ≥ 3
- Assisted reproductive technology/in vitro fertilization
- Ovarian hyperstimulation syndrome
- Multiple gestation
- Hyperemesis, dehydration
- Surgery during pregnancy
- Pre-eclampsia

Pregnancy Related Thrombosis Risk

- Antepartum
 - DVTs are most likely to be proximal and in the left leg
 - Temporary May-Thurner syndrome
- Postpartum
 - Vaginal delivery
 - Cesarean delivery

Virchow's Triad



Pregnancy Related Hypercoagulability

- Increases in Factors II, VII, VIII, X, XII
- Increase in von Willebrand Factor
- Decrease in Protein S
- Increases in PAI-1 and PAI-2 leading to decreased fibrinolysis
- Acquired resistance to activated protein C (APC) – 2nd and 3rd trimesters

Pregnancy Related Stasis

- Hormonal effects on vasculature
- Increased venous capacitance
- Decreased venous flow velocity
- Obstruction of venous return (iliac veins, inferior vena cava) by uterus
- Need for bed rest with preterm labor

Vascular Damage

- Pregnancy related
 - Endothelial damage during delivery of the fetus
- Diabetes
- Hypertension
- Trauma

Case

KV is a 32 year old woman at 28 weeks during her first pregnancy. Her past medical history includes chronic hypertension, tobacco use, and being overweight (prepregnancy BMI 29). Her family history is significant for three family members with a history of unprovoked VTE.

KV calls her OB's office with complaints of new SOB, cough, some hemoptysis, chest pain, left leg swelling and feeling sweaty all the time. She is sent to the ED for evaluation for PE.

What are the best diagnostic tests during pregnancy?

Pulmonary Embolism Symptoms in Pregnancy

- Dyspnea/SOB
- Cough
- Hemoptysis
- Pleuritic chest pain
- Tachycardia
- Tachypnea
- Fever
- Leg pain
- Leg swelling (left >> right)
- Syncope
- New fatigue
- Lower abdominal pain
- Sweating
- Unexplained hypotension

Usefulness of Risk Stratification in Pregnancy

- PERC Rule
- Wells' Criteria – high negative predictive value
- Geneva Score (revised) – excludes pregnant women
- D-dimer – pregnancy elevates D-dimer levels
- EKG

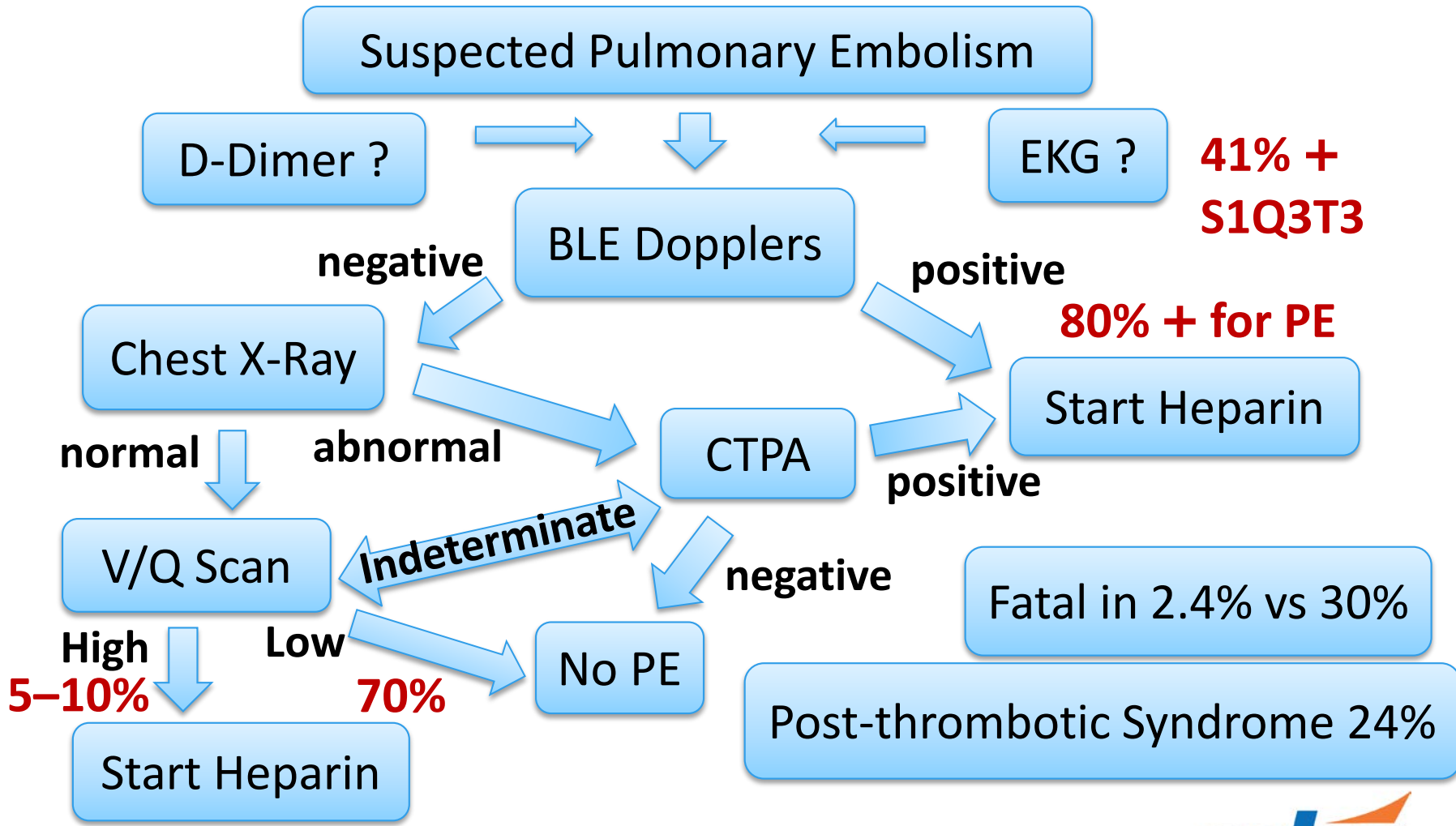
Which diagnostic test would be most helpful?

- A EKG
- B D-dimer
- C CTPA
- D V/Q Scan

D-Dimer Levels in Pregnancy

Trimester	Normal D-Dimer	PERC Cutoff Value?
First	50 – 950 ng/mL	750 ng/mL
Second	200 – 1500 ng/mL	1000 ng/mL
Third	130 – 2800 ng/mL	> 1250 ng/L
Postpartum	Peaks on 1 st day	

Decision Tree for Diagnosis



Overall < 5% Positive for PE

Other Testing for PE in Pregnancy

- CXR
- Echocardiogram
- Echocardiography
- V/Q SPECT
- MRI

Radiation Exposure

- Background radiation exposure: 1 mGy/year
- “all or none dose” – 50 – 100 mGy (5 – 10 rads)
- Chest X-ray (2 views) - < 0.01 mGy
- CTPA
 - Breast radiation higher (10 – 70 mGy)
 - Fetal radiation dose lower (0.35 – 0.66 mGy)
- V/Q scan
 - Breast radiation low (< 1.5 mGy)
 - Fetal radiation dose higher (0.64 – 0.74 mGy)

Case

KV is diagnosed with a pulmonary embolism, admitted to the hospital, and started on a heparin infusion.

The following day she develops severe hypoxia (O₂ saturation 88% on 8L NRB) and significant hypotension (55-70/38-47). An echocardiograph reveals a thrombus located in the right atrium that appears to be mobile.

What are her treatment options? The team asks you about the safety of thrombolytic therapy during pregnancy.

What are her treatment options?

- A Streptokinase
- B Tenecteplase
- C Alteplase
- D Urokinase

Thrombolysis During Pregnancy

- For women with high-risk PE (massive PE) with high risk of PE recurrence or death
 - Most cases have used alteplase
 - 10 mg bolus, 90 mg infusion over 2 hrs
 - Some cases with streptokinase and fewer used urokinase
 - Urokinase not recommended during pregnancy
- Overall complications similar to non-pregnant women

Thrombolysis During Pregnancy

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Thrombolysis in Pregnancy

- Catheter directed
 - Catheter(s) placed by interventional radiology
 - Alteplase 6 mg bolus through catheter(s), continuous infusion of 0.5 mg/hr
 - Allows for more rapid clot lysis
 - Consider in cases of intermediate-risk (submassive) PE with high risk for adverse prognosis
- No clear evidence to support systemic thrombolysis over catheter directed thrombolysis

Embolectomy During Pregnancy

- Fewer than 15 case reports
 - All performed for rapid decline in hemodynamic status or cardiogenic shock
 - Most used either cardiopulmonary bypass or cardioplegic arrest
- Consider if thrombolysis is contraindicated or has failed

Embolectomy During Pregnancy

- High maternal (15.4%) and fetal (23%) fatality rate
- Transcatheter embolectomy
 - Aspiration thrombectomy
- Method should be determined by experience of the providers

Case

KV is ready for discharge 10 days later. She is still on a heparin infusion through. What are her options for anticoagulation?

KV does well during her pregnancy until 36 weeks, when she develops preterm labor. She is admitted to the hospital again. It is a false alarm, but what about her anticoagulation this time?

KV is readmitted 2 weeks later for labor and wants an epidural. How should her anticoagulation be managed?

KV is now postpartum – how long should her therapy continue? Should she be on therapeutic or prophylactic doses?

Duration for Postpartum Therapy?

- A 3 weeks
- B 6 weeks
- C 3 months
- D 6 months

Antepartum Treatment of PE

- Low molecular weight heparin
- Fondaparinux appropriate with HIT
- When to consider warfarin?
- DOACs not appropriate during pregnancy
- Management issues at the end of pregnancy
 - Convert to subcutaneous heparin

Intrapartum Treatment of PE

- Hold heparin the evening before planned cesarean section or induction
- Hold heparin at first signs of labor (onset of contractions or rupture of membranes)
- Consider IVC filter in very high risk women
 - Recent thrombosis
 - Thrombosis on anticoagulation
- Watch timing with epidural placement/removal

Postpartum Treatment of PE

- Restart heparin 6 – 12 hours after vaginal delivery
- Restart heparin 12 – 24 hours after cesarean delivery
- Consider short-term prophylactic dose if bleeding risk high, changing back to therapeutic dosing
- Warfarin therapy appropriate for postpartum women
- DOACs are not appropriate in breastfeeding

Postpartum Treatment of PE

- Duration of therapy
 - Minimum 3 months of total therapy
 - Continue therapeutic anticoagulation throughout pregnancy
 - Continue therapy through 6 weeks postpartum
 - Treatment dose until ≥ 3 months completed
 - Prophylactic dose if treatment completed

Future Pregnancy Management

- Thrombophilia work-up?
- Prophylaxis warranted during subsequent pregnancies?

Key Takeaways

- Pregnancy significantly increases the risk of thrombosis over the general population, with the highest risk in the first week postpartum
- Thrombolysis should be considered with extensive pulmonary embolisms or life-threatening thrombi
- Duration of therapy depends on timing during pregnancy but must include at least 6 weeks postpartum

References

- Kline JA, Kabrhel C. Emergency evaluation for pulmonary embolism, part 2: diagnostic approach. *J Emer Med* 2015;49:104-117.
- Bajc M, Olsson B, Gottsater A, et al. V/P SPECT as a diagnostic tool for pregnant women with suspected pulmonary embolism. *Eur J Nucl Med Mol Imaging* 2015;42:1325-30.
- Linnemann B, Bauersachs R, Rott H, et al. Diagnosis of pregnancy-associated venous thromboembolism – position paper of the Working Group in Women’s Health of the Society of Thrombosis and Haemostasis (GTH). *Vasa* 2016;45:87-101.
- Jordan EJ, Godelman A, Levsky JM, et al. CT pulmonary angiography in pregnant and postpartum women: low yield, high dose. *Clin Imaging* 2015;39:251-3.
- Ramsay R, Byrd L, Tower C, et al. The problem of pulmonary embolism diagnosis in pregnancy. *Br J Haematol* 2015;170:727-36.

References

- Conti E, Zezza L, Ralli E, et al. Pulmonary embolism in pregnancy. *J Thromb Thrombolysis* 2014;37:251-70.
- Brennan MC, Moore LE. Pulmonary embolism and amniotic embolism in pregnancy. *Obstet Gynecol Clin N Am.* 2013;40:27-35.
- Chau DF, Fragneto RY. Maternal embolism. *Int Anesthes Clin* 2014;52:61-84.
- Goodacre S, Nelson-Piercy C, Hunt, B, Chan W-S. When should we use diagnostic imaging to investigate pulmonary embolism in pregnant and postpartum women? *Emerg Med J* 2015;32:78-82.
- Kline JA, Richardson DM, Than MP, et al. Systematic review and meta-analysis of pregnant patients investigated for suspected pulmonary embolism in the emergency department. *Acad Emer Med* 2014;21:949-59.
- Tatebe S. Cardiologists and the management of obstetric venous thromboembolism. *Circ J* 2015;79:1215-7.

References

- Konkle BA. Diagnosis and management of thrombosis in pregnancy. Birth Defect Res (Pt C) 2015;105:185-9.
- James AH. Thrombosis in pregnancy and maternal outcomes. Birth Defect Res (Pt C) 2015;105:159-66.
- Bloom AI, Farkas A, Kalish Y, et al. Pharmacomechanical catheter-directed thrombolysis for pregnancy-related iliofemoral deep vein thrombosis. J Vasc Interv Radiol 2015;26:992-1000.
- Saeed G, Möller M, Neuzner J, et al. Emergent surgical pulmonary embolectomy in a pregnant woman: case report and literature review. Tex Heart Inst J 2014;41:188-94.
- Linnemann B, Scholz U, Rott H, et al. Treatment of pregnancy-associated venous thromboembolism – position paper of the Working Group in Women’s Health of the Society of Thrombosis and Haemostasis (GTH). Vasa 2016;45:103-118.

References

- Pick J, Berlin D, Horowitz J, et al. Massive pulmonary embolism in pregnancy treated with catheter-directed tissue plasminogen activator. *A&A Case Reports* 2015;4:91-4.
- Casazza F, Caponi C, Mignoli S. A four-chamber in transit heart thrombus in a pregnant woman with acute pulmonary embolism. *Thromb Haemost* 2015;114:5-6.
- Açar G, Şimşek Z, Avcı A, et al. Right heart free-floating thrombus in a pregnant woman with massive pulmonary embolism: a case of 'emboli in transit'. *J Cardiovasc Med* 2015;16:S51-4.
- Fasullo S, Scalzo S, Marighini G, et al. Thrombolysis for massive pulmonary embolism in pregnancy: a case report. *Am J Emer Med* 2011;29:698.e1-698.e4.
- Tawfik MM, Taman ME, Motawea AA, Abdel-Hady E. Thrombolysis for the management of massive pulmonary embolism in pregnancy. *Int J Obstet Anesth* 2013;22:149-52.



Pulmonary Embolism During Pregnancy

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**Caring for Two in the ICU:
Critical Illness in Pregnancy
A Focus on Maternal Cardiac Arrest**

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Emergency Medicine Pharmacist

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“CODE OB, ER, STAT”

“I’m fine.”

34 y/o F

29 weeks

BP 90/60

HR 145

RR 24

O₂ sat 96% RA

Temp 98.3°F



I regularly respond to obstetric emergencies within my institution.

A Yes

B No

I received formal training to respond to obstetric emergencies within my institution.

A Yes

B No



Research Article

Management of Maternal Cardiac Arrest in the Third Trimester of Pregnancy: A Simulation-Based Pilot Study

Crit Care Res Pract 2016 [Epub ahead of print].

1:12,000

58.9%

“Two-fer”

Anesthesiology 2014; 120:810-818.
Circulation 2015; 132:1747-1773.

Part 12: Cardiac Arrest in Special Situations

**2010 American Heart Association Guidelines for Cardiopulmonary
Resuscitation and Emergency Cardiovascular Care**

Circulation 2010; 122[Suppl]:S829-S861.

AHA Scientific Statement

Cardiac Arrest in Pregnancy

A Scientific Statement From the American Heart Association

Circulation 2015; 132:1747-1773.

An anatomical illustration of a human heart, showing the major arteries and veins. The heart is rendered in a realistic, reddish-pink color. Overlaid on the left side of the heart are four semi-transparent, dark red rectangular boxes, each containing white text. The text in the boxes, from top to bottom, is: 'Shunt', 'Increase CO', 'Reduced AVR', and 'Progesterone'.

Shunt

Increase CO

Reduced AVR

Progesterone

Crit Care Clin 2004; 20:609-615.
Surg Clin North Am 2008; 88:391-401.
Clin Obstet Gynecol 1996; 39:3-16.

MV = 1.5x

TLC

Residual

Progesterone

pH 7.4 to 7.47 | PaO₂ 104 to 108 | PaCO₂ 30 to 32 | HCO₃²⁻ 15 to 20



Clin Chest Med 1992; 13:555-565.

CHEST 2015; 148:1093-1104.



Early Warning Score

Class I, Level C

Specific to OB

Anaesthesia 2013; 68:354-367.
Circulation 2015; 132:1747-1773.

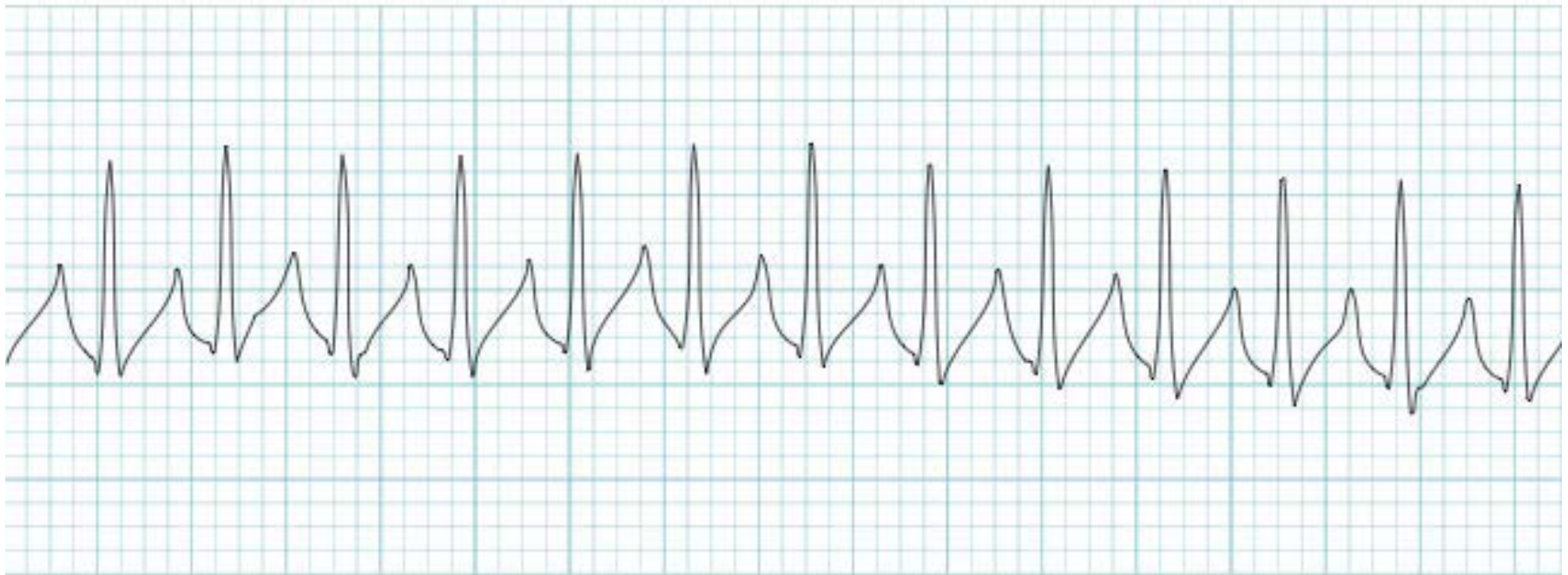
	3	2	1	0	1	2	3
SBP	< 80	80-89		90-139	140-149	150-159	≥ 160
DBP				< 90	90-99	100-109	≥ 110
RR	< 10			10-17	18-24	25-29	≥ 30
HR	< 60			60-110		111-149	≥ 150
% O₂ for SpO₂ ≥ 96%				RA	24-39%		≥ 40%
T (°C)	< 34.0		34.0-35.0	35.1-37.9	38.0-38.9		≥ 39
AMS				No			Yes

0	Routine (12-hour observation)
1-3 (aggregate)	4-hour observation
Single 3 or ≥ 4 (aggregate)	1-hour observation and urgent team involvement
≥ 6 (aggregate)	Continuous observation and emergent team involvement

Anaesthesia 2013; 68:354-367.
 Circulation 2015; 132:1747-1773.

BP 90/60 | HR 145 | RR 24 | O₂ sat 96% RA | T 98.3°F
SBP: 0 | DBP: 0 | HR: 2 | RR: 1 | %O₂ for SpO₂ ≥ 96%: 0 | T: 0

While you call OB, who calls NICU...



EKG courtesy of Life in the Fast Lane (LITFL)

What intervention will you recommend to correct this patient's abnormal cardiac rhythm?

- A** Direct current cardioversion
- B** Adenosine
- C** Metoprolol
- D** Diltiazem



AVNRT

Atrial tachycardia

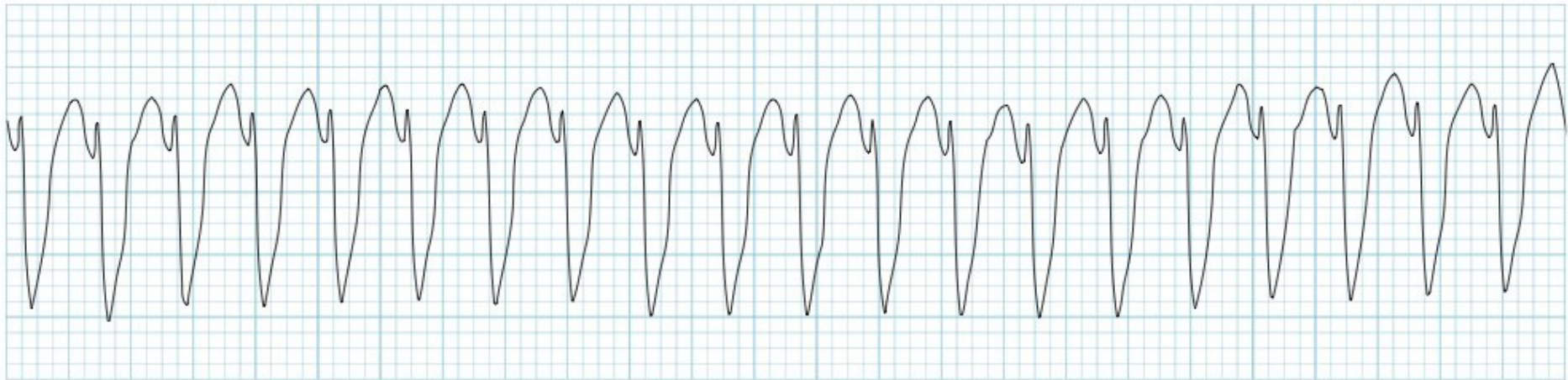
WPW

J Obstet Gynaecol Can 2011; 33:17-23.
Circ Arrhythm Electrophysiol 2014; 7:961-967.

BP 86/55 | HR 155 | RR 30 | O₂ sat 96% 8 L NC | T 100.3°F

“My heart feels funny.”

“I...can barely...breathe...”



EKG courtesy of Life in the Fast Lane (LITFL)

What medications will you prepare to draw up for this pregnant patient in cardiac arrest?


- A** Magnesium
- B** Epinephrine
- C** Vasopressin
- D** None, since she is pregnant; I will charge the paddles in case an electric shock is indicated.

Tilt: Left lateral decubitus

Oxygen: HFNC >> NIV

Lines: Above diaphragm

Dates/Delivery

Courtesy of Haney Mallemat ( @CriticalCareNow)
Circulation 2015; 132:1747-1773.



Techniques for Left Uterine Displacement

Circulation 2010; 122[Suppl]:S829-S861.



4+ responders

100/min, 30:2

Sternum up

“Shock advised?”

Circulation 2015; 132:1747-1773.

Br J Anaesth 2001; 87:237-239.



Bleeding/DIC

Embolism

Anesthetic complications

Uterine atony

Cardiac disease

Hypertension/(Pre)eclampsia

Other: Differential per ACLS

Placental abruption

Sepsis

Circulation 2010; 122[Suppl]:S829-S861.



ABW / IBW / PBW

ADME

Categories (pre 12/2014)

“Real world”

Safety

Nat Rev Cardiol 2015; 12:718-729.
N Engl J Med 1998; 338:1128-1137.

Medication for Rapid Sequence Intubation	Pregnancy Category	Comments
Premedications		
Lidocaine	B	<ul style="list-style-type: none"> Lidocaine and its metabolite (MGX) both cross the placenta No teratogenic effects demonstrated in animal studies
Fentanyl	C	<ul style="list-style-type: none"> Toxicity to embryo and fetus demonstrated during in animal studies Fentanyl does cross the placenta, but IV formulation has been used safely during labor May be associated with respiratory depression of the fetus if used near delivery
Induction Agents		
Midazolam	D	<ul style="list-style-type: none"> Midazolam and its metabolite (α-hydroxymidazolam) crosses the placenta and detectable levels have been found in amniotic fluid No teratogenic effects demonstrated in animal studies No reports describing its use in the 1st and 2nd trimesters
Etomidate	C	<ul style="list-style-type: none"> Has been shown to cross the placenta in animal studies Has been used as general anesthetic for cesarean delivery No reports describing its use in the 1st and 2nd trimesters
Ketamine	Not officially defined ("D")	<ul style="list-style-type: none"> Ketamine can cross the placenta May produce uterine contractions (dose-dependent) No teratogenic effects demonstrated in animal or human studies
Propofol	B	<ul style="list-style-type: none"> Propofol crosses the placenta May be associated with central nervous system and respiratory depression of the neonate No reports describing its use in the 1st and 2nd trimesters
Paralytic Agents		
Succinylcholine	C	<ul style="list-style-type: none"> Small amounts of succinylcholine can cross the placenta No reports of teratogenic effects Pregnancy may be associated with decrease in activity of plasma cholinesterase, which may result in increased sensitivity to the agent
Rocuronium	C	<ul style="list-style-type: none"> Limited placental transfer due to the presence of quaternary ammonium group Not recommended by the manufacturer for use in rapid sequence induction during cesarean delivery No teratogenic effects demonstrated in animal studies
Vecuronium	C	<ul style="list-style-type: none"> Small amounts of vecuronium can cross the placenta Studies have not been conducted for its use during reproduction or organogenesis Appears to pose little risk to developing fetus when used in 2nd and 3rd trimesters



Emergency Medicine PharmD. [Preventing the Burn: Safety of RSI Medications in Pregnancy.](#)

14 March 2013.

“Medication doses do not require alteration to accommodate the physiological changes of pregnancy.”

“Although there are changes in the volume of distribution and clearance of medication during pregnancy, there are very few data to guide changes in current recommendations.”

“In the setting of cardiac arrest, no medication should be withheld because of concerns about fetal teratogenicity.”

“Physiological changes in pregnancy may affect the pharmacology of medications, but there is no scientific evidence to guide a change in current recommendations.”

“Therefore, the usual drugs and doses are recommended during ACLS.”

Circulation 2015; 132:1747-1773.

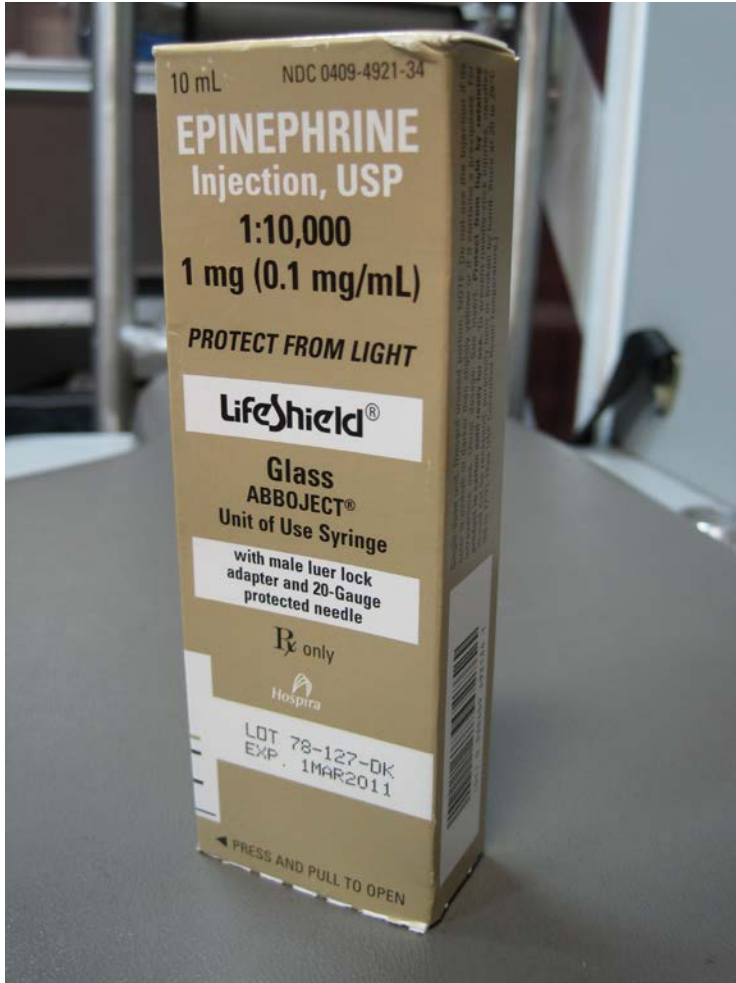


Even Amiodarone?

“For refractory (shock-resistant) ventricular fibrillation and tachycardia, amiodarone 300 mg rapid infusion should be administered with 150-mg doses repeated as needed.”

Circulation 2015; 132:1747-1773.

“



>>



”

Circulation 2015; 132:1747-1773.
Am J Obstet Gynecol 1994; 171:1634-1642.

Drug error

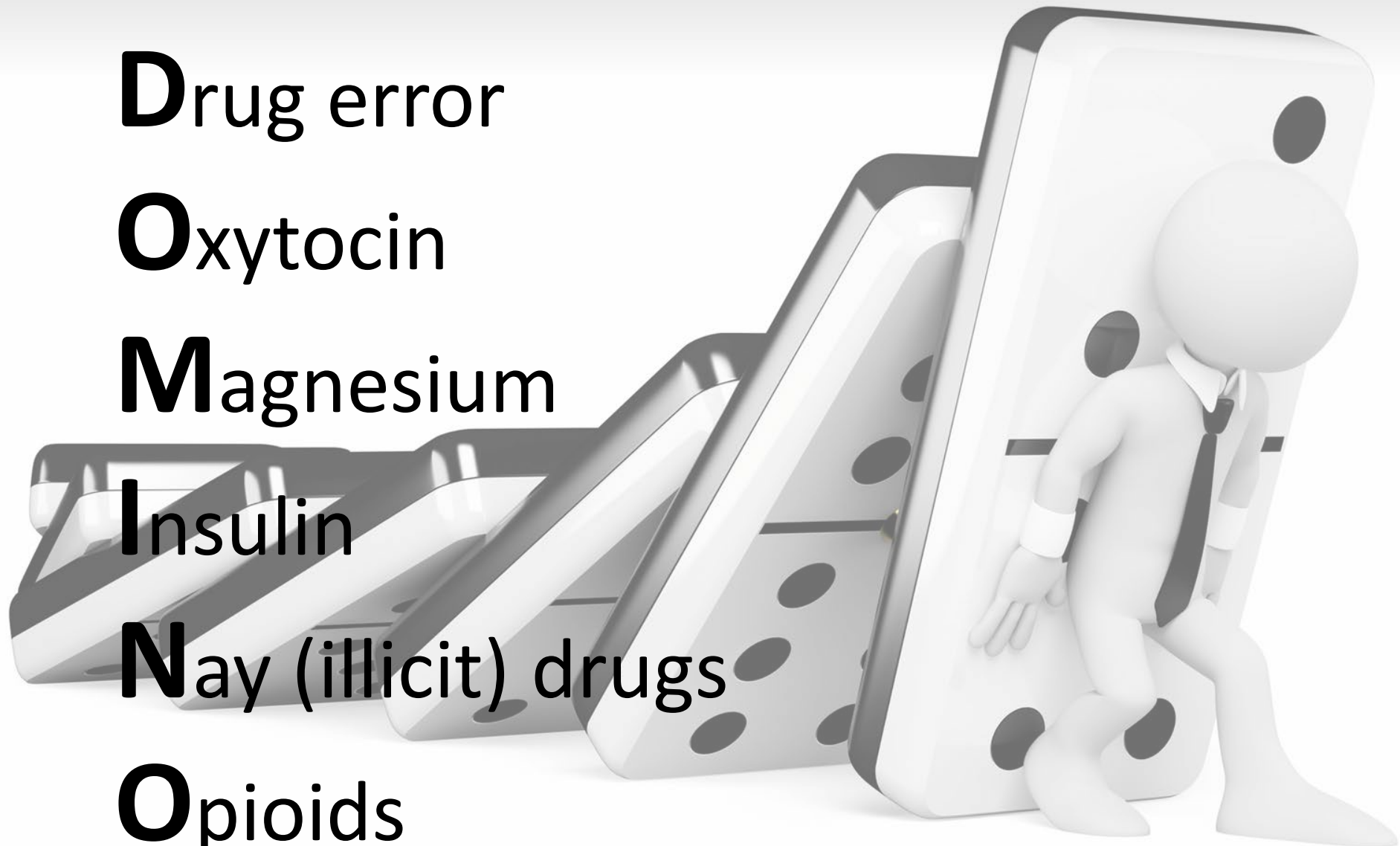
Oxytocin

Magnesium

Insulin

Nay (illicit) drugs

Opioids



Circulation 2015; 132:1747-1773.

Bolus: 1.5 mL/kg (W?)

ROSC:

Infusion:

0.25 mL/kg/min

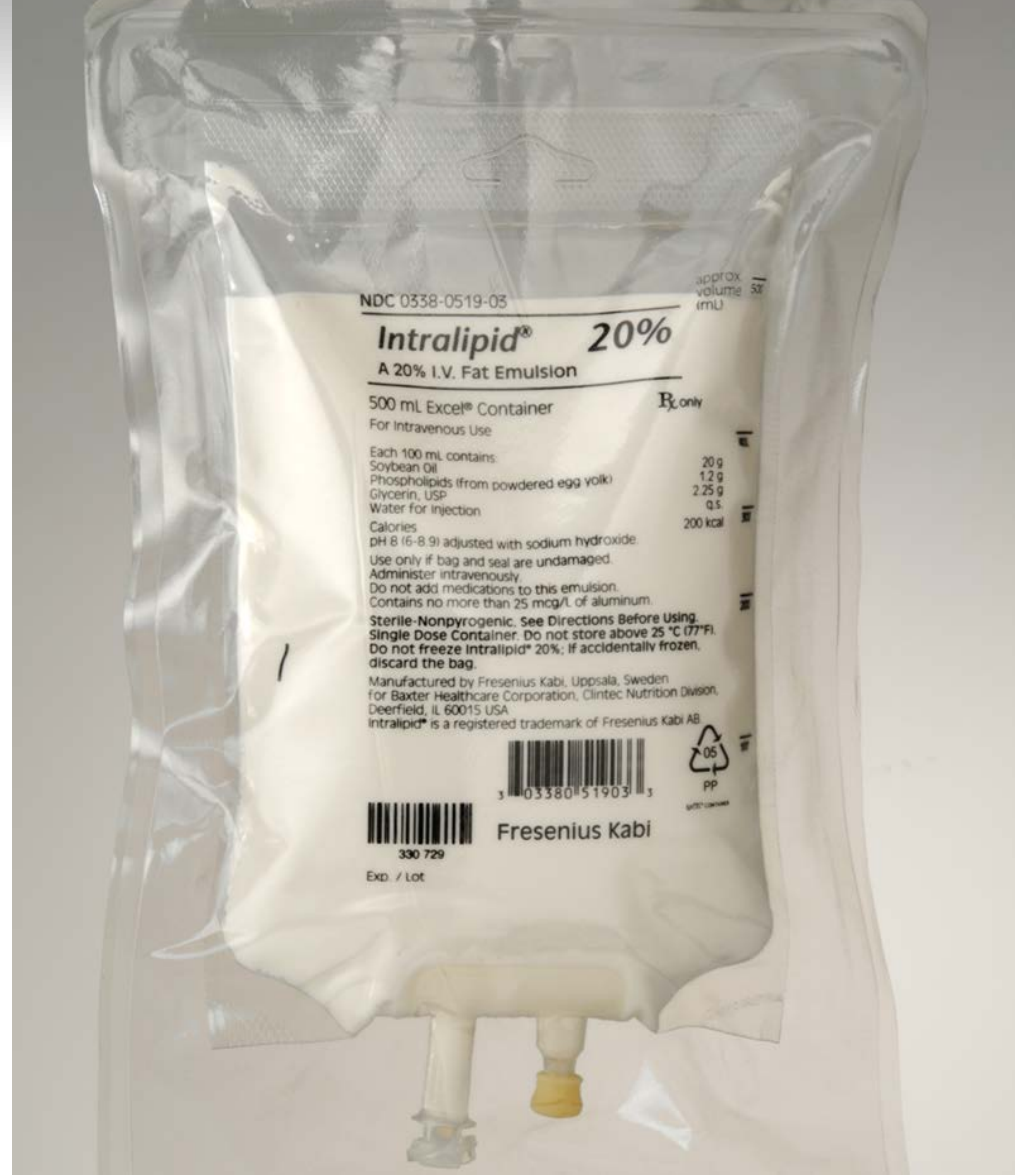
10+ minutes

No ROSC:

Re-bolus AND

Infusion:

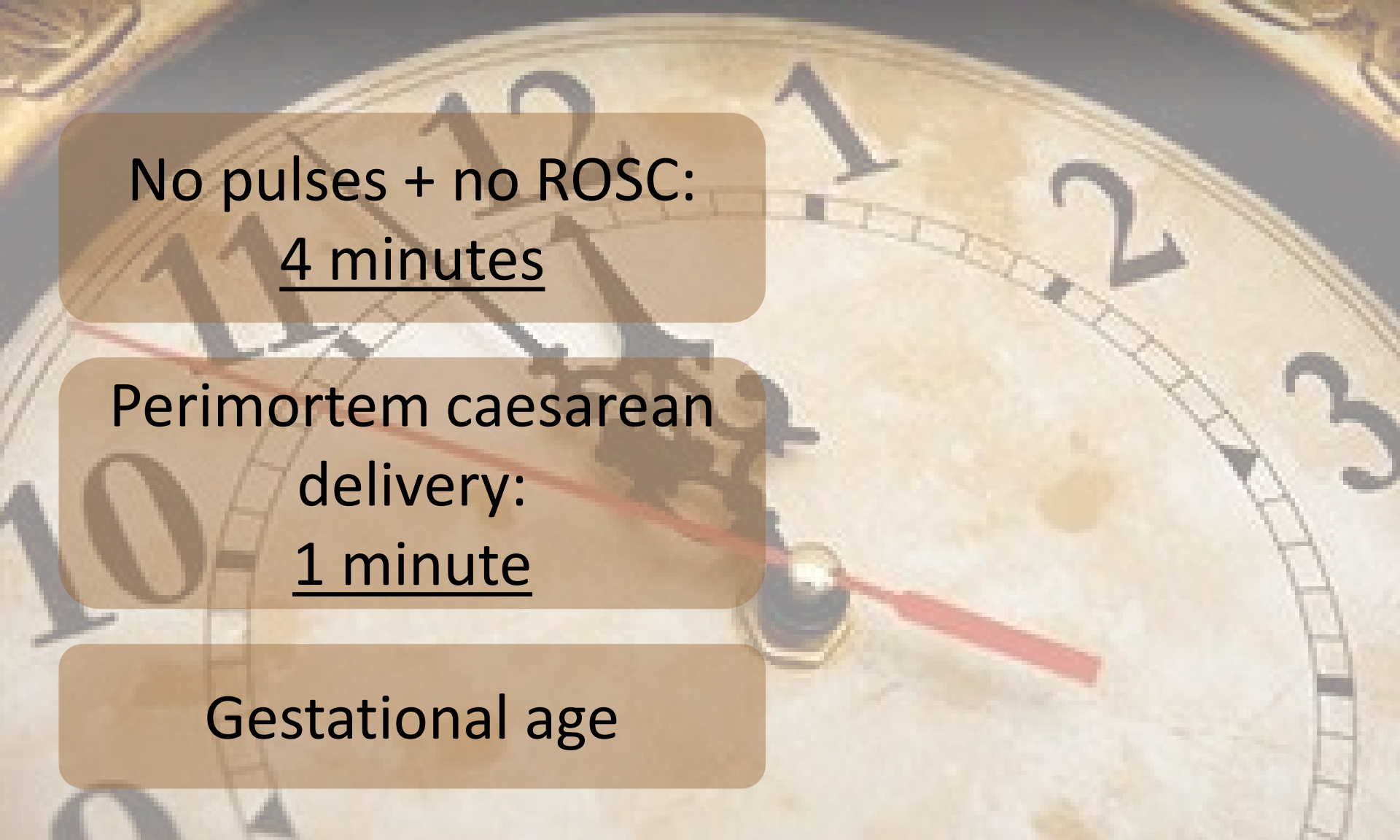
0.5 mL/kg/min



Circulation 2015; 132:1747-1773.

Clin Toxicol 2016; 54:167-193.

Clin Toxicol 2016 [Epub ahead of print].



No pulses + no ROSC:
4 minutes

Perimortem caesarean
delivery:
1 minute

Gestational age

Am J Obstet Gynecol 2005; 192:1916-1920.

Resuscitation 2012; 83:1191-1200.

Circulation 2015; 132:1747-1773.

A person in a red jacket and black gear is climbing a massive, blue-tinted ice wall. The ice has a complex, layered texture with many cracks and ridges. The person is positioned near the bottom right of the frame, providing a sense of scale to the enormous ice formation.

Not contraindicated

Success in 3 cases

Individual basis

Crit Care Med 2008; 36:1354-1356.

Ann Emerg Med 2012; 60:786-789.

Tex Heart Inst J 2015; 42:367-371.

SUMMARY

1. Multidisciplinary approach to maternal cardiac arrest (**YOU**, too).
2. Causes: BEAUCHOPS, DOMINO.
3. CPR, TOLD: Keys to survival.
4. “Any and all” medications can be given in maternal cardiac arrest.





**Caring for Two in the ICU:
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A Focus on Maternal Cardiac Arrest**

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It's Not Just Gestational...
The Recognition and Management of the
Preeclampsia Spectrum

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Disclosures

- I have no relevant financial relationships or commercial interests to disclose for this presentation
- Medications discussed in the presentation may be for off-label indications

Objective

- Distinguish between the treatment strategies related to preeclampsia and associated complications.
 - Briefly discuss the epidemiology and pathophysiology of preeclampsia
 - Explain the preeclampsia “spectrum”, including definitions of early and severe disease
 - Review medication related treatment strategies for hypertension (HTN) in pregnancy and preeclampsia and their potential impact on maternal and fetal health in the acute setting

The Incidence of Preeclampsia

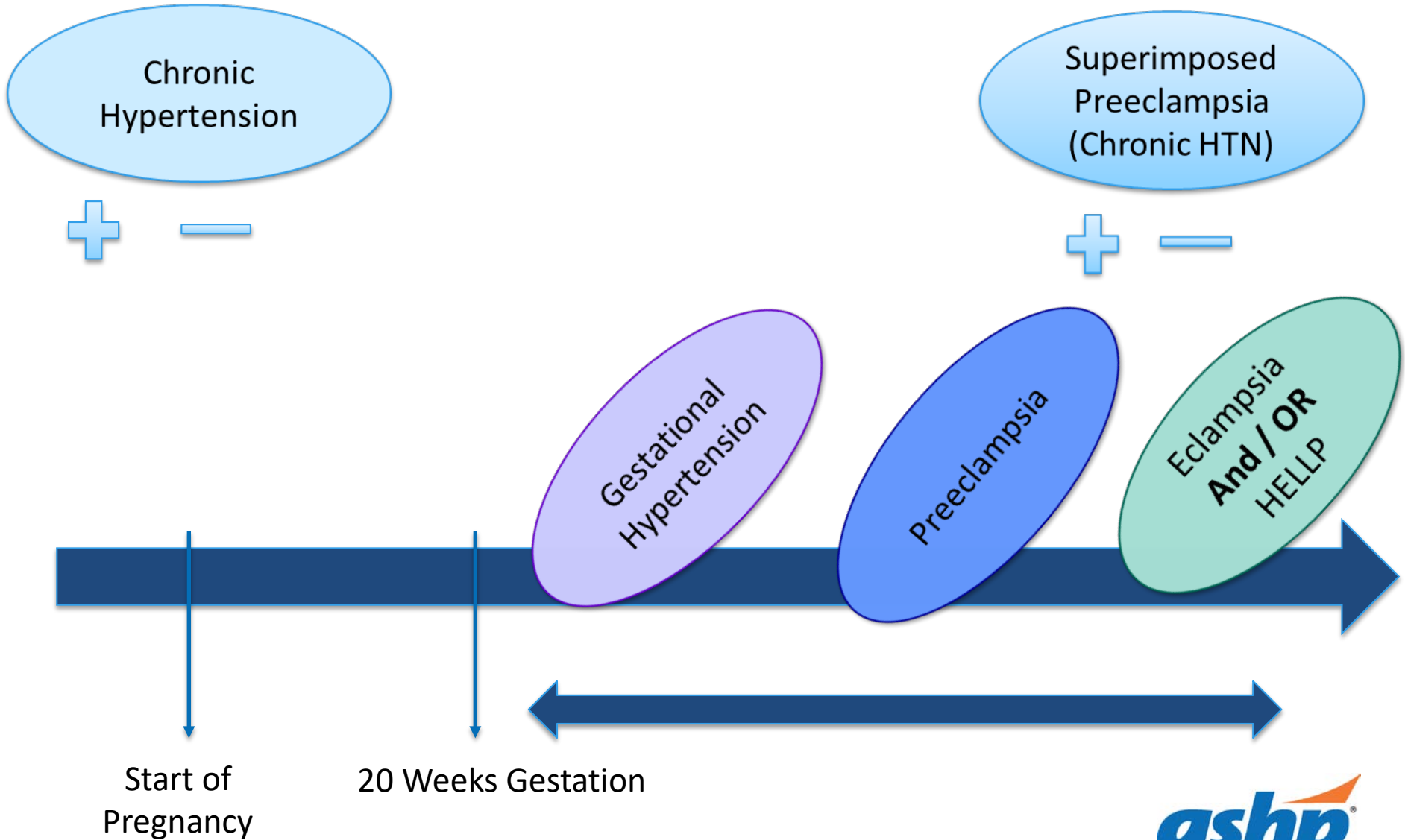
- Worldwide, preeclampsia affects about 10 million births annually
- Mortality - Approximately 76,000 maternal deaths and 500,000 babies each year
- Developed Countries
 - Hypertensive disorders of pregnancy are associated with 5-8% of U.S. births
 - Incidence of preeclampsia is estimated at 2-5% in U.S., Canada, and Western Europe
- Developing Countries
 - Incidence varies anywhere from 4-18% in other parts of world, including Africa and Latin America

Gestational Hypertension	<ul style="list-style-type: none"> • New onset elevations of BP after 20 weeks gestation in the absence of proteinuria • Unresolved HTN postpartum should be reclassified as <i>Chronic HTN</i>
Chronic Hypertension	<ul style="list-style-type: none"> • High BP known to predate conception or detected before 20 weeks gestation
Preeclampsia	<ul style="list-style-type: none"> • New onset hypertension AND <ul style="list-style-type: none"> • New onset proteinuria OR • In the absence of proteinuria, PLT count <100,000 • Elevated LFTs (2x normal) • New renal insufficiency (SCr >1.1 or 2x baseline) • Pulmonary edema • New onset cerebral or visual disturbances
Eclampsia	Convulsive phase of disease (often preceded by headaches, hyperreflexia)
Superimposed Preeclampsia	<ul style="list-style-type: none"> • HTN in early gestation with development of proteinuria after 20 weeks OR • Proteinuria before 20 weeks gestation and evidence of organ dysfunction or severe HTN

Hypertension = systolic BP \geq 140 or diastolic BP \geq 90, or both

Severe Hypertension = systolic BP \geq 160 or diastolic BP \geq 110, or both

“Spectrum” of Disease



Pathophysiology

- 2000 years, and we still don't exactly know, but what we do know is hypertension is the most common initial manifestation rather than the primary cause
- Leading pathophysiologic processes thought to contribute to preeclampsia:
 - Immunologic
 - Placental implantation
 - Endothelial dysfunction
 - Angiogenic Factors
 - Genetics

Fetal Impact

- *In utero*
 - Fetal demise or “still birth” are reported at a rate of 21 per 1000 births in severe preeclampsia
 - Intrauterine growth restriction
- Neonatal thrombocytopenia / Neutropenia
- Bronchopulmonary dysplasia
- Questionable impact on neurodevelopmental issues
 - Potential reduced risks of cerebral palsy and interventricular hemorrhage
 - Unclear impact on infant development
- Potential increased risk for late adult disease states
 - Diabetes, Obesity, Cardiovascular Disease

Maternal Impact

- Potential Immediate Complications
 - Eclampsia
 - HELLP (hemolysis, elevated liver enzymes, low platelet count)
 - Disseminated intravascular coagulation
 - Cardiopulmonary complications
- Long Term Complications
 - Increased risk of recurrent disease with subsequent pregnancies
 - Increased cardiovascular and cerebrovascular morbidity and mortality risks

Challenges

The key is EARLY!!!! Identification and treatment initiation

- Early identification of at risk patients
- Distinguishing hypertension types in pregnant patients
- Initiation of appropriate monitoring and treatment upon diagnosis
- Diagnosis of post-partum preeclampsia
- Balance of maternal –fetal morbidity and mortality risks with fetal development and maturation *in utero*
- Medication management and it's impact on both mother and baby

How does this present in the ED

- Unfortunately this can be challenging to diagnose in the ED setting
 - Any patient > 20 weeks gestation with HTN, should be assessed for both proteinuria and other diagnostic criteria previously mentioned, including signs and symptoms on presentation and physical exam
- Can potentially present with eclampsia
- Can potentially present post-partum up to 4-6 weeks and still be at risk, so thorough HPI / PMH and any associated symptoms may aid in diagnosis

Treatment Strategy Overview

- Gestational HTN and preeclampsia without severe features
 - Delivery for women at 37 0/7 weeks is the safest and most appropriate strategy to ensure both maternal health and mature fetal development
 - Close monitoring for women before 37 0/7 weeks with no signs of acute fetal distress or growth restriction requiring delivery
- Preeclampsia with severe features at 34 0/7 weeks or greater and / or unstable maternal – fetal conditions, should be stabilized and delivery as soon as possible
-So where is the pharmacy in this?

Please tell me there are Guidelines!!

- The American College of Obstetricians and Gynecologists (ACOG) convened a Hypertension in Pregnancy Task Force in 2011
 - A review of existing evidence to develop guideline recommendations
 - An evaluation of areas of clinical research that are lacking and should be pursued
- Other guideline documents include the Royal College of Obstetricians and Gynecologists (NICE), Society of Obstetricians and Gynecologists of Canada, Society of Obstetric Medicine of Australia and New Zealand

Anti-Hypertensive Therapy

- Indicated for severe gestational HTN management
- The role in mild HTN is not clear, and risk of fetal harm may outweigh benefits
 - If administered enteral options include labetalol, IR or XR nifedipine

Drug	Dose	Max Dose	Comment(s)
Labetalol	20 mg IV, and repeat escalating doses every 10 min	220 mg	Avoid in reactive airway disease and heart failure
Hydralazine	5 or 10 mg IV, followed by a repeat dose of 10 mg x 1 in 20 min	20-30 mg	Can cause sudden hypotension and tachycardia - consider 500 mL fluid bolus
Nifedipine IR	10 mg PO, followed by 10 or 20 mg PO in 20 min, may repeat x 1	10-50 mg	Some variability between guidelines; Avoid in CAD, aortic stenosis



Anti-Hypertensive Therapy

For refractory patients... 2nd line therapies include

Drug	Dose*	Max Dose*	Comment(s)
Labetalol	Titratable infusion	160 mg/hr	If patient was not responsive to intermittent bolus may not be beneficial
Nicardipine	Titratable infusion	10 mg/hr	2 nd line – minimal risk
Sodium Nitroprusside	Titratable infusion	< 4 hours exposure	Increased risk for fetal cyanide toxicity, should be last-line option
Nitroglycerin	Titratable infusion	100 mcg/min	May be a good choice for patients with pulmonary edema

* **Dose and Max Dose** may vary based on institutional restrictions

Anti-Hypertensive Therapy

- Review by Sebastiaan et.al.
 - 140 total patients from 5 studies
 - 91% successfully reduced MAP by 20%
 - 70% within 20 min of initiation (90% within 130 min)
 - 8 pts with transient maternal hypotension and 2 fetal decelerations captured
- RCT by Elatrous et.al.
 - 63% of labetalol vs. 70% of nicardipine achieved their target goals within 11 and 12 min respectively
 - No hypotension in either group
 - Mild tachycardia in nicardipine group
 - One transient deceleration in the labetalol group

Magnesium Sulfate

- MOAs:
 - NMDA receptor antagonist
 - Calcium antagonist
 - Decreased BBB permeability
- Magnesium's role as a primary strategy for seizure management was evaluated by the Eclampsia Trial Collaborative Group
- Goal magnesium levels are 3.5-5 mEq/L and unclear correlation
- Safety Concerns
 - Maternal concerns include hypermagnesemia toxicity
 - Does magnesium mask convulsant activity rather than treat it?
 - Fetal hyporeflexia and respiratory depression

Magnesium Sulfate

- Prophylaxis
 - In patients without severe features of preeclampsia, available data suggests there is no role for prophylactic treatment
 - In patients with severe features, specifically neurologic disturbances, clonus, or right upper quadrant pain, prophylaxis is warranted
- Treatment
 - All patients presenting with eclamptic convulsions should receive immediate treatment
- Dosing Strategy
 - IV: 4-6 gram loading dose with 1-2 grams/ hr continuous infusion
 - IM: 10 gram IM (5 gram each buttock)

Corticosteroids

- Evidence supporting the use of antenatal corticosteroids has been available for decades
 - Improves fetal lung maturation and reduces the risk of respiratory distress in the neonatal period
- Historically recommended for all women at 24-34 weeks gestation as a single course within 7 days of delivery, or repeated doses if > 2 weeks
- Updated recommendations from ACOG also address late preterm role of corticosteroids and their benefit
 - Monitoring neonatal glucose is recommended
- If patients are considered late preterm and have already received antenatal corticosteroid therapy, a second dose is not necessary

Potential Complications and Pitfalls

- Magnesium
 - Prolongs the duration of smooth muscle relaxation associated with non-depolarizing paralytic agents in the OR
 - Hemodynamic affects that are exaggerated by anti-hypertensive therapy
 - Laboratory monitoring and interpretation
- Anti-hypertensive therapy
 - In conjunction with anesthetics can increase the risk of severe hypotension
- Evidence of thrombocytopenia may impact the ability to provide spinal anesthesia
- Limit maintenance fluids

What to Monitor

- Maternal Monitoring
 - Hypo- and hypertensive episodes
 - Cardiovascular status
 - Evidence of magnesium toxicity
 - Symptoms concerning for eclampsia
 - Laboratory changes/ symptoms consistent with HELLP
- Fetal Monitoring
 - Evidence of fetal distress

Summary

- Optimizing maternal health both prior to and early in pregnancy is key to minimizing risk
- Early identification of HTN in the second trimester
- Frequent monitoring and BP stabilization
- Magnesium as appropriate to prevent/ treat seizures
- Antenatal corticosteroids
- Post partum evaluation and monitoring
- Secondary prophylaxis for subsequent pregnancies

The Key Role of EM/OB/ICU Pharmacists

- Thorough history to help identify at risk patients
- Early introduction of pharmacologic interventions as appropriate
- Assessment of fetal risk associated with drug therapy
- Alternative routes of administration
- Therapeutic drug monitoring and adjustment as necessary

True or False

A TRUE

B FALSE

All women with preeclampsia, regardless of symptoms, should receive magnesium sulfate therapy upon admission to the hospital for BP management



It's Not Just Gestational...
The Recognition and Management of the
Preeclampsia Spectrum

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Caring for Two in the ICU: Managing Critical Illness in Pregnancy

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