University of Colorado **Anschutz Medical Campus**

HYPOVENTILATION, HYPOXIA, AND HYPERCAPNIA OH MY! PULMONARY DISORDERS IN PREGNANCY

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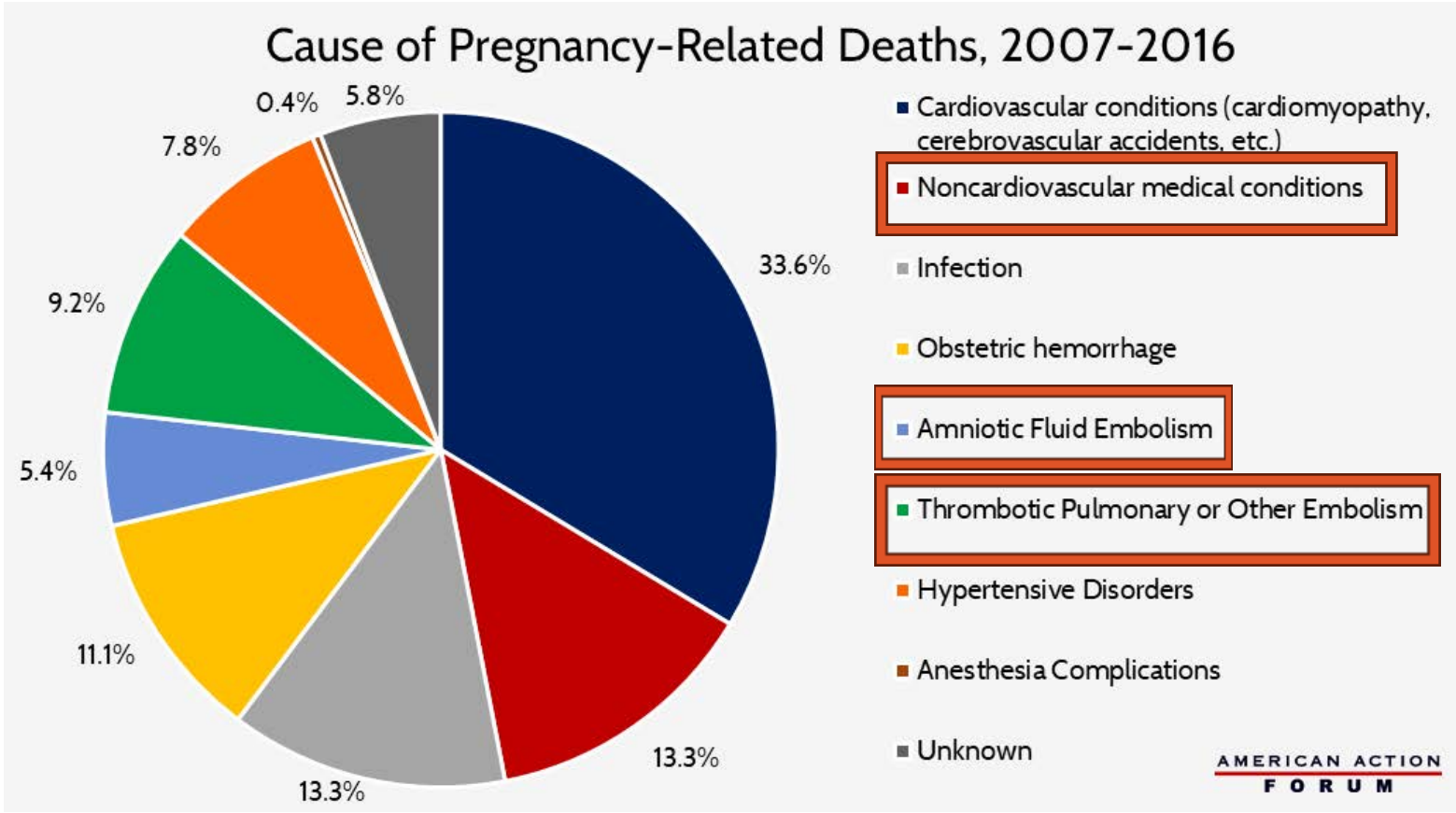
Disclosures

- None

Objectives

- Impact on maternal morbidity and mortality
- Physiologic pulmonary adaptations in pregnancy
  - Oxygenation
  - Ventilation
  - Placental gas exchange
- Pathophysiology of pulmonary disease in pregnancy
  - Asthma
  - Pulmonary embolism
  - Pneumonia
  - ARDS
  - Tuberculosis
  - Cystic fibrosis
  - Pulmonary hypertension

Maternal Mortality

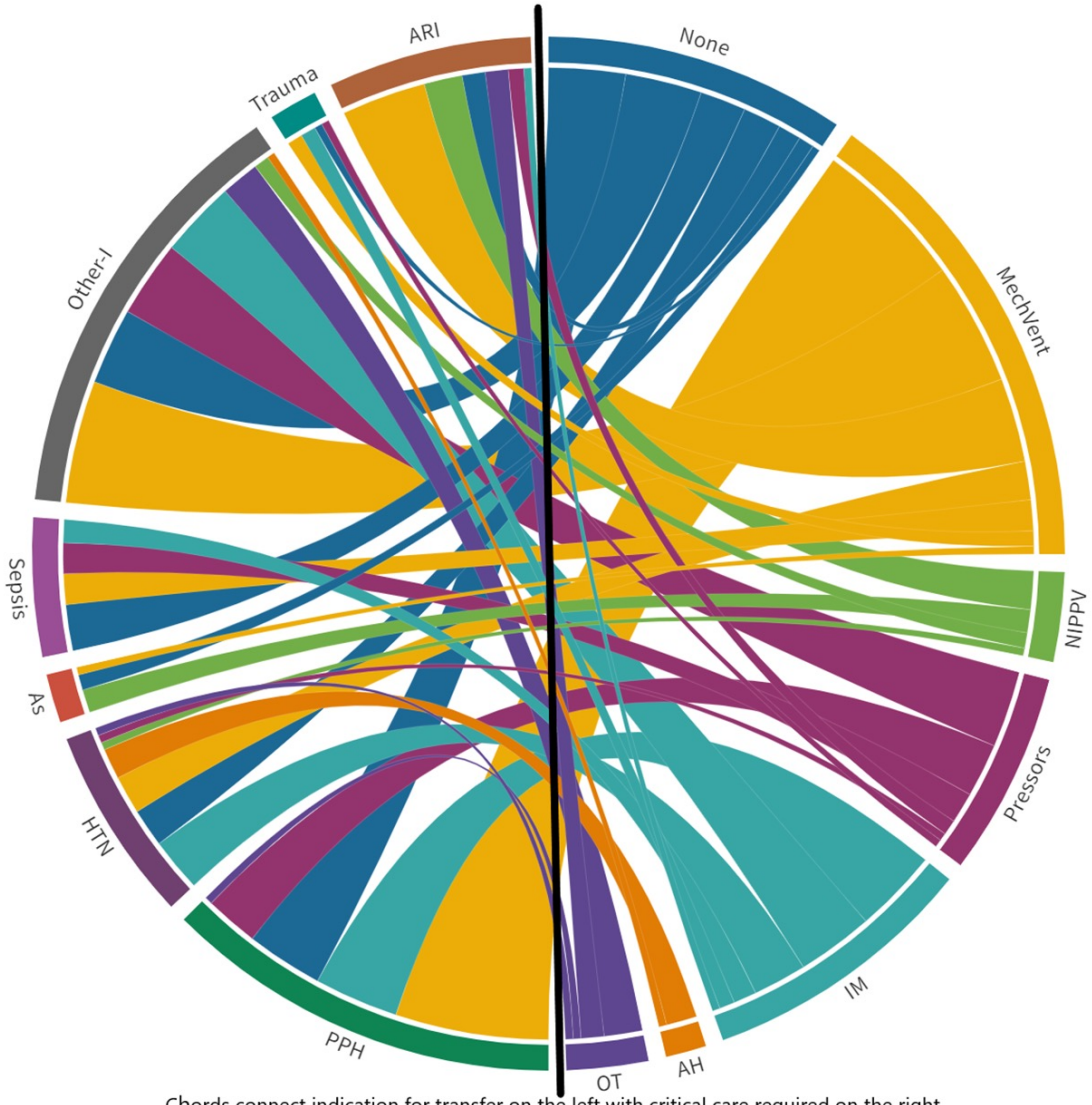


Indications for ICU admission

102 ICU admissions over a 5-year period at a single center

Indication for transfer	N=102 (%)	Critical Care Required	N=102 (%)
Hemorrhage	32 (31)	None	29 (28)
Hypertension	16 (16)	Invasive Ventilation	48 (47)
Respiratory Insufficiency	20 (20)	Non-Invasive Ventilation	9 (9)
Sepsis	15 (15)	Vasopressor infusion	19 (19)
Trauma	4 (4)	Antihypertensive infusion	4 (4)
Other	34 (33)	Invasive Hemodynamic Monitoring	28 (28)
		Other	7 (7)

Figure 1: Indication for transfer and critical care provided



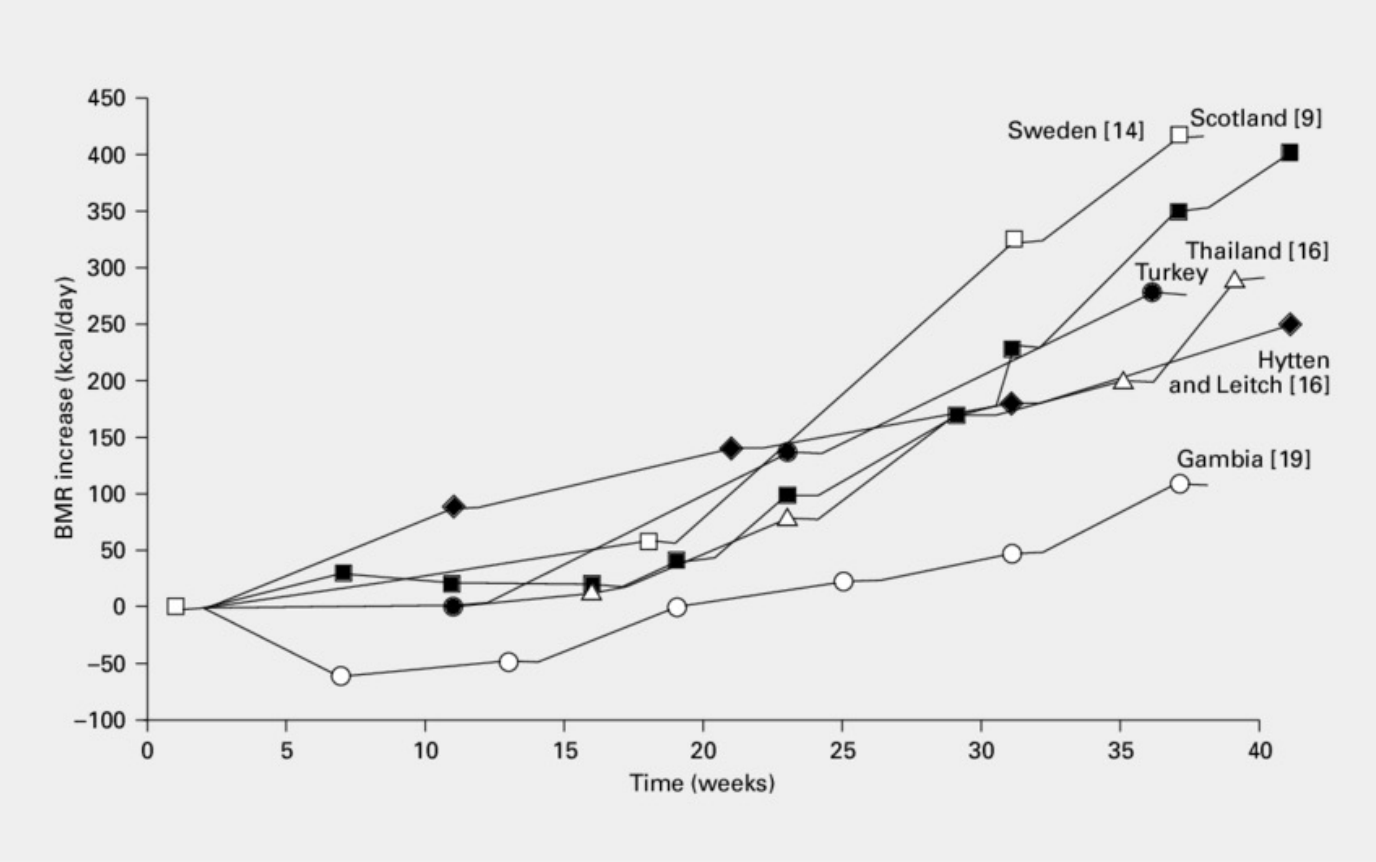
Chords connect indication for transfer on the left with critical care required on the right

ARI=Acute respiratory insufficiency, Other-I=Other indication for transfer, As=Asthma, HTN=Hypertension, PPH=Hemorrhage, OT=Other treatment, AH=Antihypertensive infusion, IM=Invasive monitoring, NIPPV=Non-invasive positive pressure ventilation

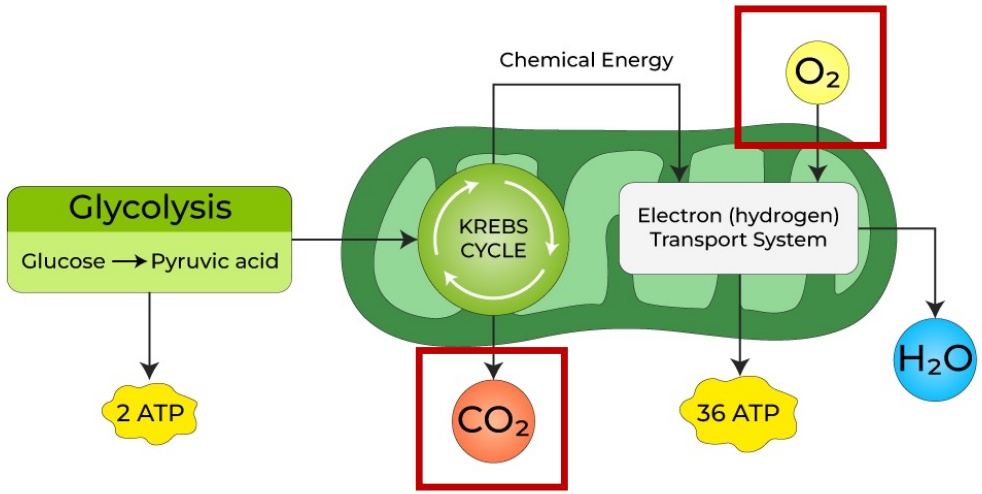
Metabolic demands of pregnancy

Basal metabolic rate

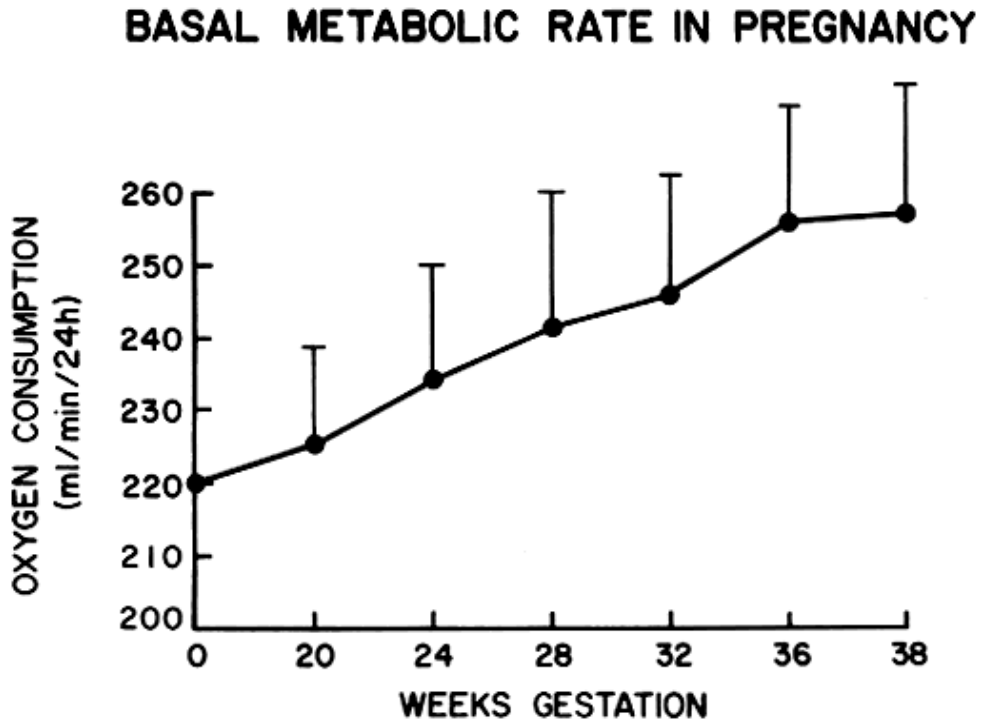
- BMR increases by 20-60% in pregnancy
- “Metabolism for two”



Metabolic demands of pregnancy



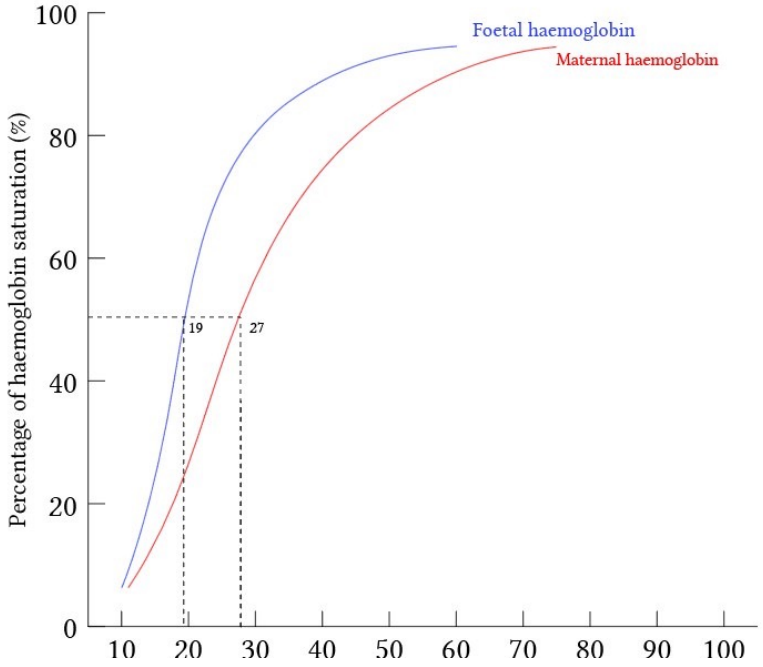
"Breathing for two"

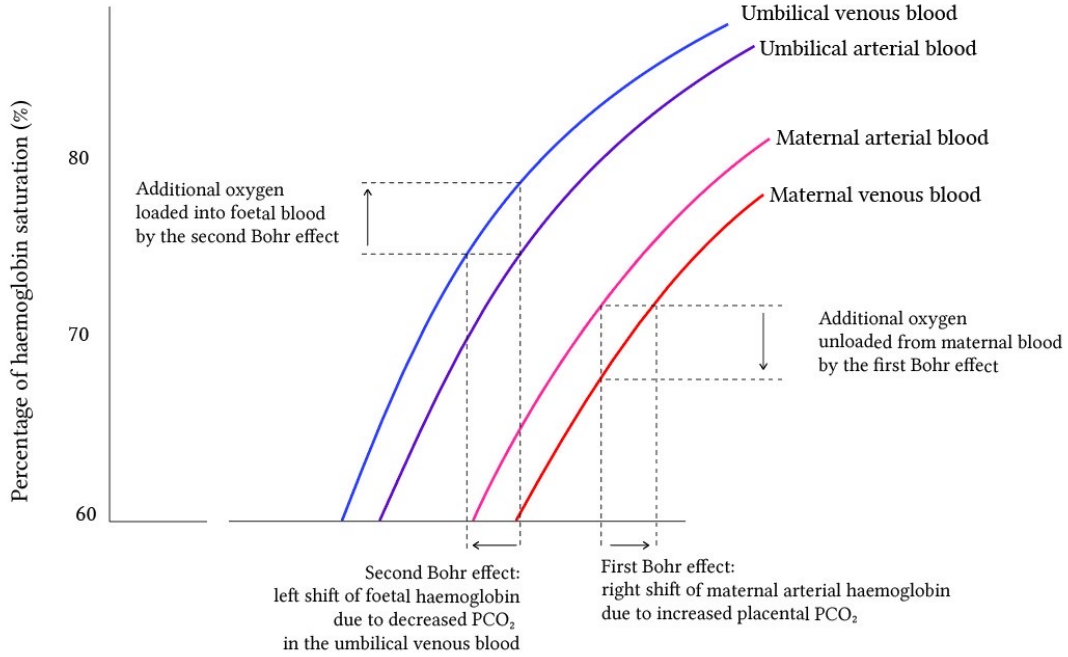


Oxygen delivery

Fetal cheat codes

- Fetal Hgb has higher O2 affinity
- Resp alk increases 2-3 DPG aiding O2 offloading
- Fetal Hgb averages 15g/dL at term
- Oxygen delivery is largely driven by SpO2 not PaO2

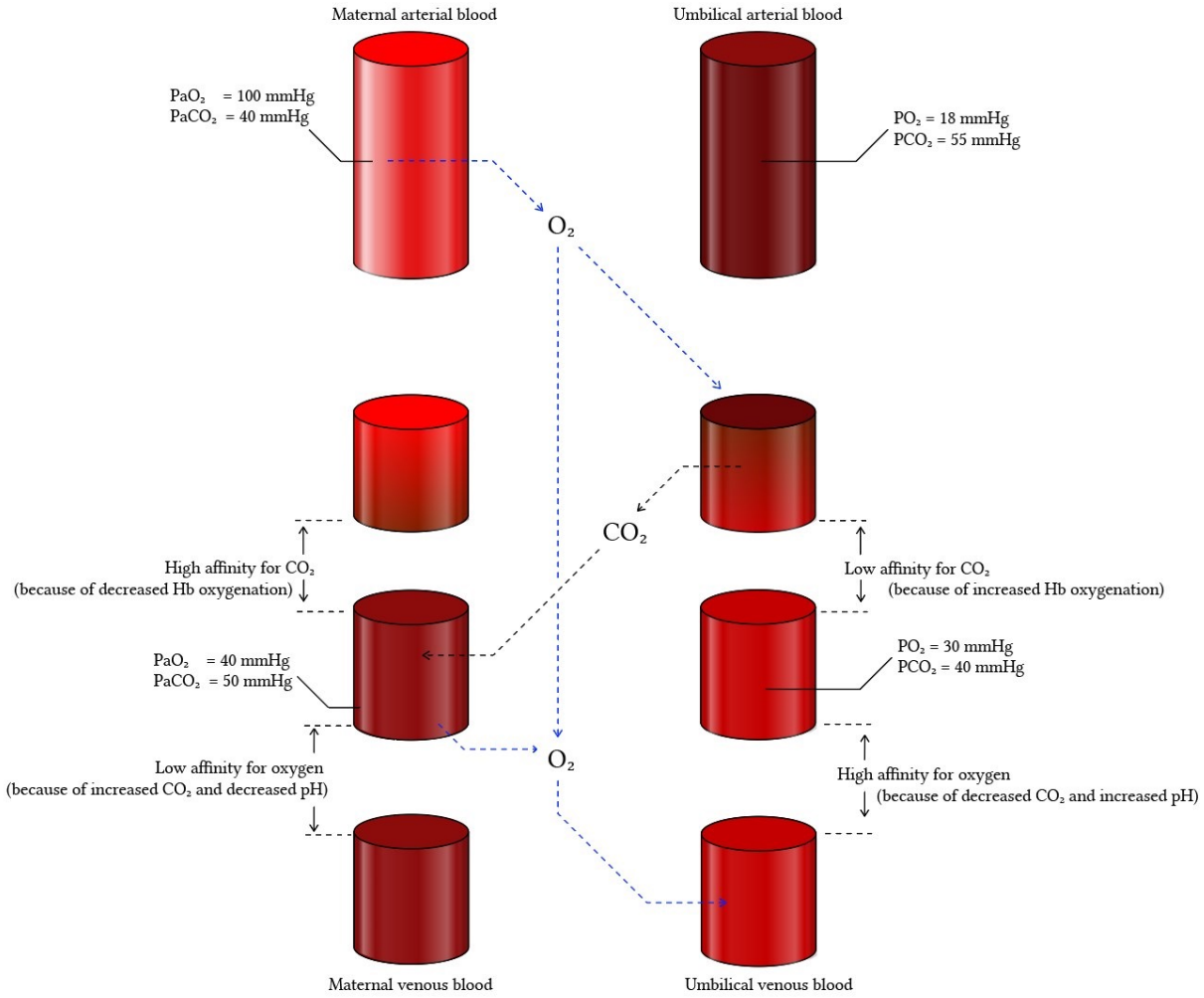




Carbon dioxide offloading

Gradient dependent

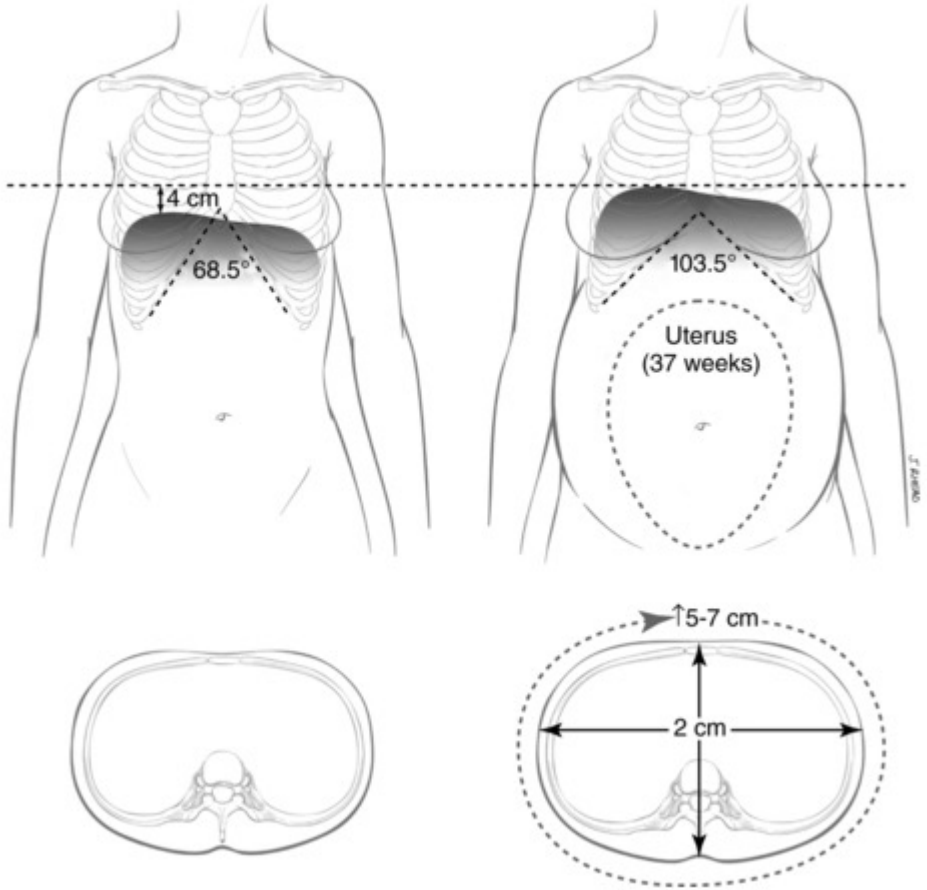
- CO2 must move from high to low concentration
- Increased maternal ventilation leads to decreased PCO2 levels
- Compensated respiratory alkalosis



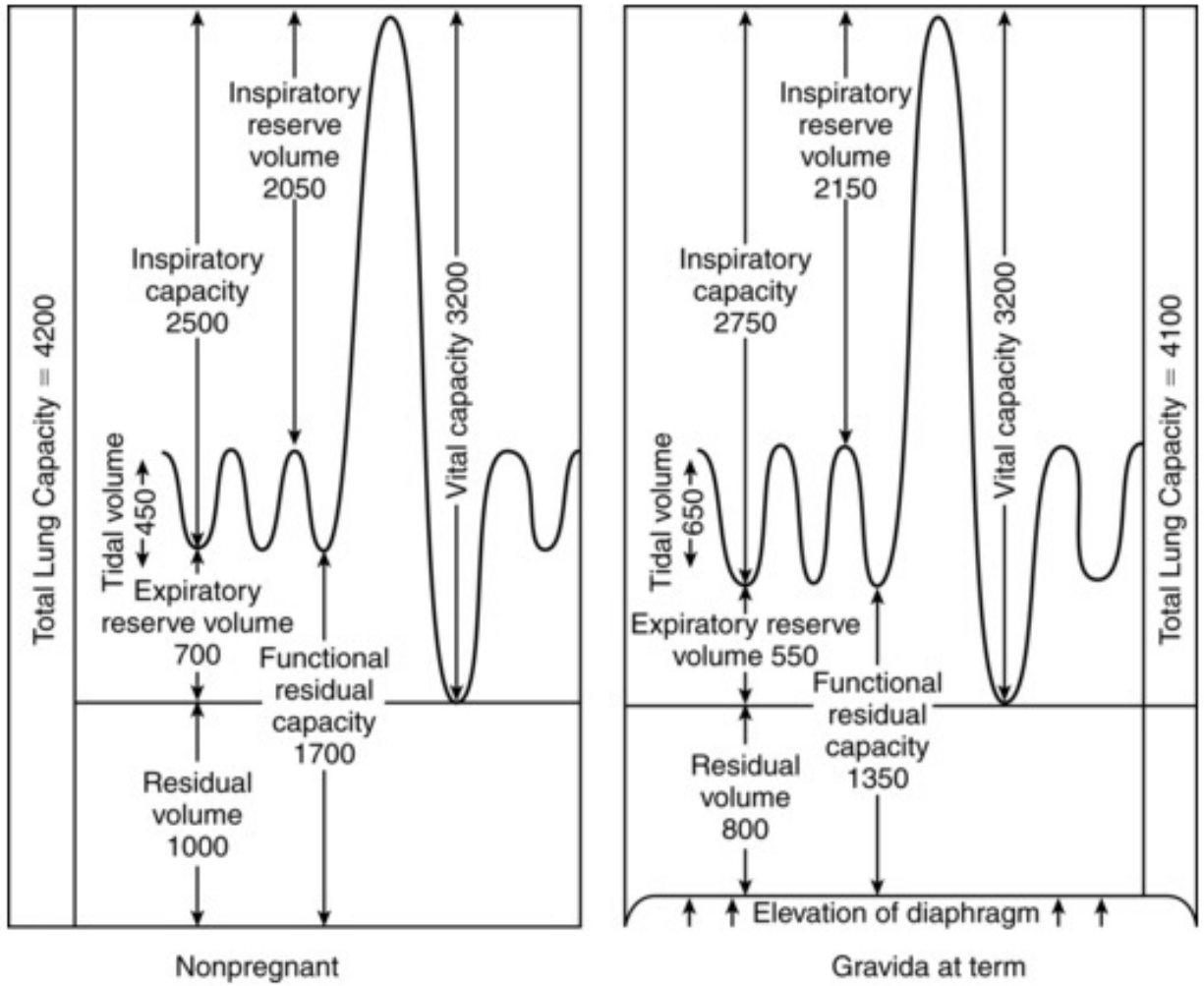
Respiratory Alkalosis

Blood gas measurement	Non-pregnant adult	Third trimester
pH	7.38–7.44	7.39–7.45
Arterial partial pressure of oxygen (mmHg [kPa])	80–100 (11–13)	92–107 (12.3–14.3)
Arterial partial pressure of carbon dioxide (mmHg [kPa])	35–45 (4.7–5.9)	25–33 (3.3–4.4)
Bicarbonate (mmol/L or mEq/L)	21–30	16–22

Physiologic changes in pregnancy

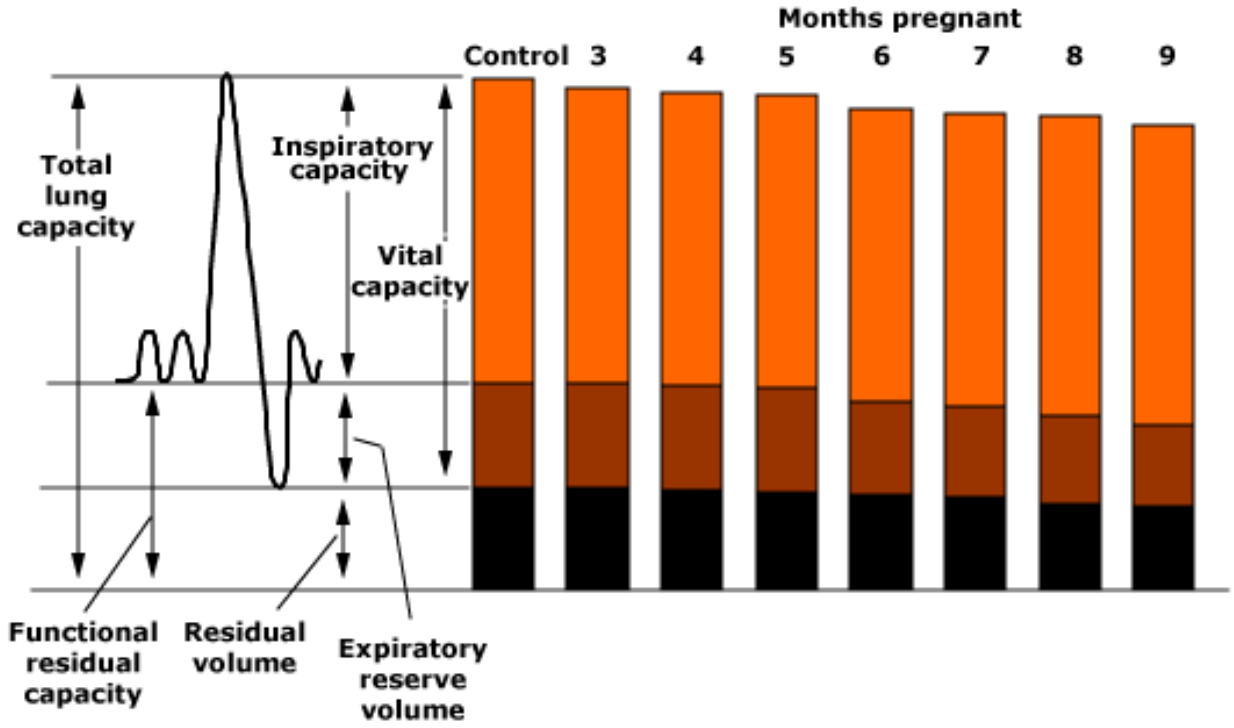


Hegewald, M.J. & Crapo, R.O. (2011). Respiratory physiology in pregnancy. *Clin Chest Med*, 32, 1.



Thorax	
Chest wall compliance	Decreased
Thoracic diameter	Increased
Diaphragm	Elevated
Lung compliance	Unchanged
Lung Volumes	
Total lung capacity	Slightly increased
Vital capacity	Slightly increased
Inspiratory capacity	Slightly increased
Functional residual capacity	Decreased
Residual volume	Slightly decreased
Expiratory reserve volume	Decreased
Spirometry	
FEV1, FVC, FEV1/FVC	Unchanged
Ventilation	
Minute ventilation	Increased
Tidal volume	Increased
Respiratory rate	Unchanged
Blood gas	
pH	Normal
PaO2	Slightly elevated (100-105 mmHg)
PaCO2	Slightly decreased (32-34 mmHg)
Bicarbonate	Slightly decreased (15-21 mmHg)

Changes in pulmonary function tests during pregnancy



Serial measurements of lung volume compartments during pregnancy. Functional residual capacity decreases approximately 20 percent during the latter half of pregnancy, due to a decrease in both expiratory reserve volume and residual volume.

Redrawn from Prowse, CM, Gaensler, EA, Anesthesiology 1965; 26:381.

UpToDate®

Respiratory disease in pregnancy

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Asthma

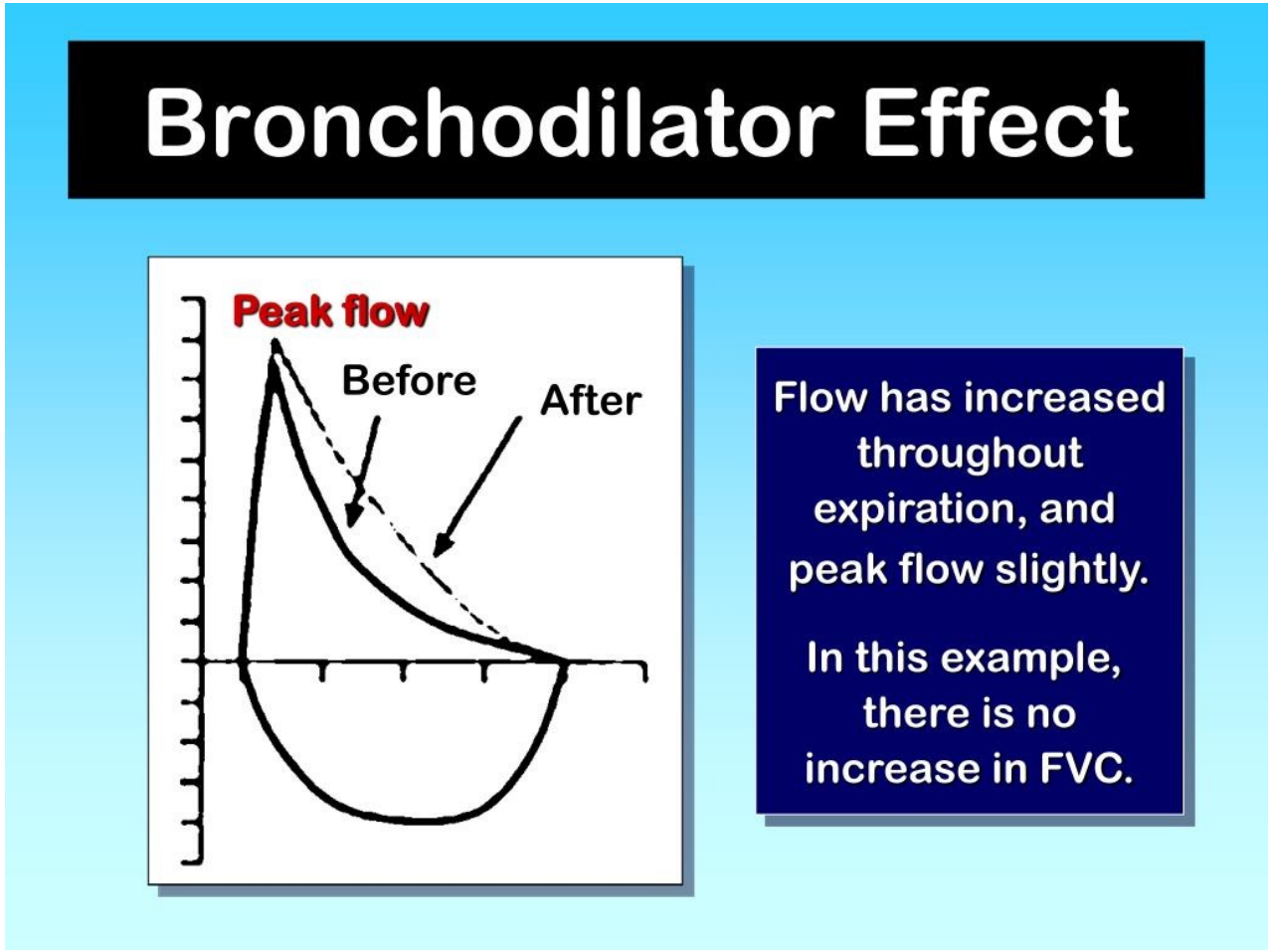
Reactive airway disease

- Chronic airway inflammation with increased responsiveness to stimuli leading to airway obstruction
- Complicates 4-8% of pregnancies
- Increasing prevalence and morbidity

Asthma

Diagnosis

- Signs and symptoms: Cough, wheezing, chest tightness, dyspnea
- Typically enter pregnancy with a diagnosis
- Dx is made when FEV1 is reduced at baseline but improves by greater than 12% with bronchodilator administration
- PFTs are safe in pregnancy
- Methacholine testing is not advised
- Consider testing for IgE antibodies to specific triggers

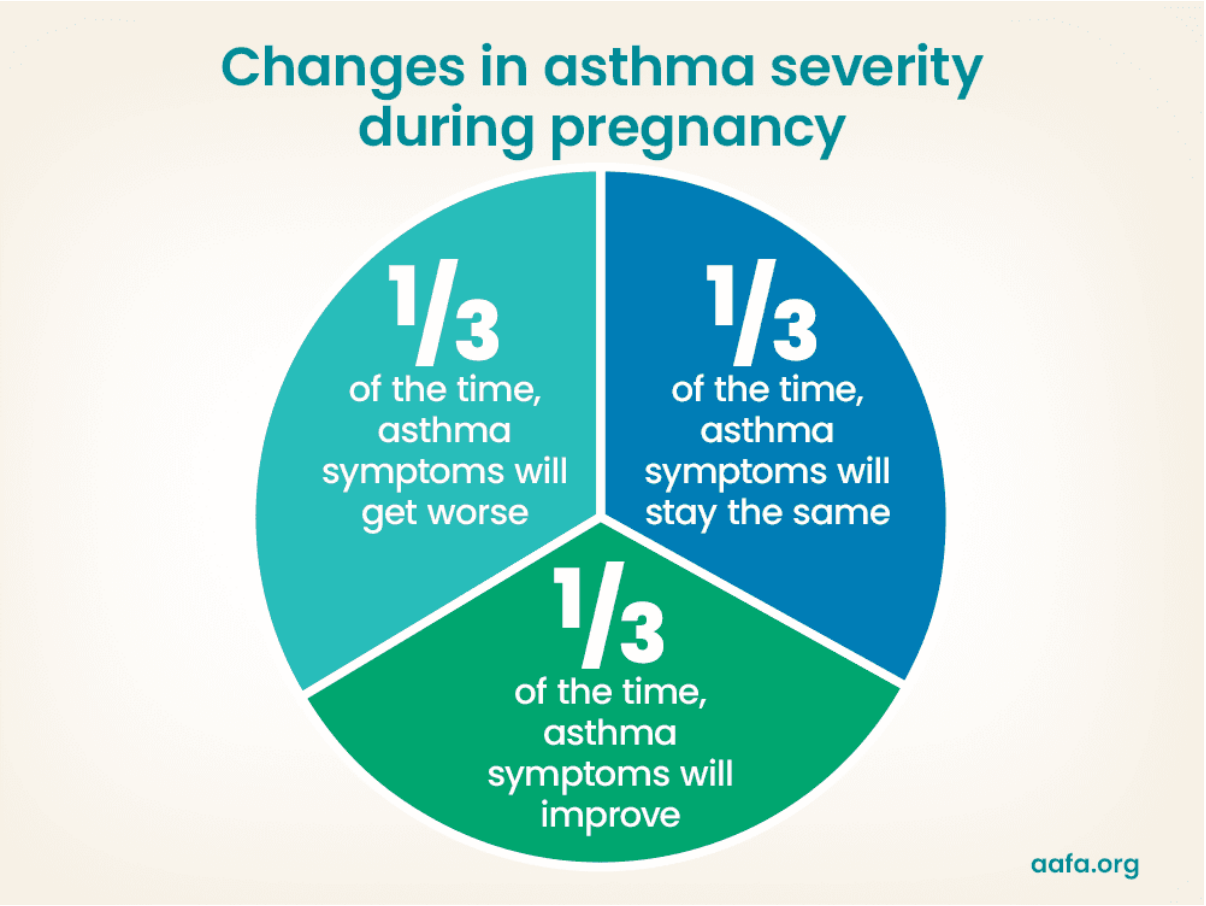


Components of Severity		Classification of Asthma Severity (Youths ≥12 years of age and adults)			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment **Normal FEV_1/FVC:** **8–19 yr 85%** **20 –39 yr 80%** **40 –59 yr 75%** **60 –80 yr 70%**	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3–4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not >1x/day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV_1 between exacerbations • FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 ≥80% predicted • FEV_1/FVC normal	• FEV_1 >60% but <80% predicted • FEV_1/FVC reduced 5%	• FEV_1 <60% predicted • FEV_1/FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year (see note)	≥2/year (see note) →		
		← Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. →			
		Relative annual risk of exacerbations may be related to FEV_1			

Asthma

Effects of pregnancy on asthma

- Mild
  - 12.6% exacerbation
  - 2.3% hospitalization
- Moderate
  - 25.7% exacerbation
  - 6.8% hospitalization
- Severe
  - 51.9% exacerbation
  - 26.9% hospitalization



Asthma

Effects of asthma on Pregnancy

TABLE 3
Singleton pregnancy complications among US women with asthma

Outcomes	No asthma n = 206,468 n (%)	Asthma n = 17,044 n (%)	Site-adjusted *P* value[a]	Site-adjusted odds ratio (95% CI)[a]	Fully adjusted odds ratio (95% CI)[a,b]
Hypertensive disorders of pregnancy					
Superimposed preeclampsia	1680 (0.8)	213 (1.3)	< .0001	1.54 (1.33–1.79)	1.34 (1.15–1.56)
Eclampsia	207 (0.1)	33 (0.2)	.01	1.61 (1.10–2.36)	1.41 (0.96–2.07)
Preeclampsia	9628 (4.7)	924 (5.4)	< .0001	1.24 (1.16–1.33)	1.14 (1.06–1.22)
Gestational hypertension	5523 (2.7)	557 (3.3)	.0003	1.18 (1.08–1.30)	1.08 (0.98–1.19)
Maternal seizure					
All maternal seizures	176 (0.1)	33 (0.2)	.0008	1.93 (1.32–2.83)	1.79 (1.21–2.63)
Maternal seizure without hypertension noted	93 (0.05)	14 (0.09)	.19	1.45 (0.83–2.55)	1.35 (0.77–2.37)
Maternal seizure with hypertension noted	83 (0.05)	19 (0.12)	.0006	2.51 (1.48–4.25)	2.37 (1.40–4.02)
Other pregnancy complications					
Gestational diabetes	10,420 (5.1)	927 (5.4)	.06	1.07 (1.00–1.15)	1.11 (1.03–1.19)
Chorioamnionitis	6415 (3.1)	504 (3.0)	.32	1.05 (0.95–1.16)	1.06 (0.96–1.17)
Placenta previa	1444 (0.7)	141 (0.8)	.06	1.19 (0.99–1.42)	1.30 (1.08–1.56)
Complications of labor and delivery					
Prelabor cesarean delivery	23,688 (11.5)	2193 (12.9)	< .0001	1.15 (1.10–1.21)	1.16 (1.09–1.23)
Spontaneous labor	111,523 (54.0)	8921 (52.3)	< .0001	0.86 (0.84–0.89)	0.87 (0.84–0.90)
Cesarean delivery after spontaneous labor	18,835 (9.1)	1749 (10.3)	.0003	1.10 (1.05–1.16)	1.06 (1.00–1.12)
Induction	71,257 (34.5)	5930 (34.8)	< .0001	1.10 (1.06–1.13)	1.10 (1.06–1.14)
Cesarean delivery after induction	14,746 (7.1)	1381 (8.1)	< .0001	1.22 (1.15–1.29)	1.17 (1.10–1.24)
All vaginal delivery	149,199 (72.3)	11,721 (68.8)	< .0001	0.84 (0.81–0.87)	0.84 (0.80–0.87)
PPROM	4596 (2.2)	516 (3.0)	< .0001	1.23 (1.12–1.36)	1.18 (1.07–1.30)
PROM	14,379 (7.0)	1212 (7.1)	.98	1.00 (0.94–1.07)	0.99 (0.93–1.05)
Breech presentation	8785 (4.3)	811 (4.8)	.01	1.10 (1.02–1.19)	1.13 (1.05–1.22)
Placental abruption	3242 (1.6)	380 (2.2)	< .0001	1.27 (1.14–1.42)	1.22 (1.09–1.36)
Maternal hemorrhage	13,423 (6.5)	1292 (7.6)	.001	1.11 (1.04–1.18)	1.09 (1.03–1.16)
Maternal pulmonary embolism	114 (0.06)	20 (0.12)	.008	1.90 (1.18–3.07)	1.71 (1.05–2.79)
Maternal postpartum fever	5531 (2.7)	532 (3.1)	.35	1.05 (0.95–1.15)	0.99 (0.90–1.09)
Maternal ICU admission	902 (0.6)	73 (0.6)	.01	1.38 (1.08–1.76)	1.34 (1.04–1.72)
Maternal death	18 (0.01)	1 (0.01)	.70	Not calculated	Not calculated
Low birthweight, <2500 g	16,551 (8.1)	1815 (10.7)	< .0001	1.26 (1.19–1.33)	1.16 (1.10–1.23)
Preterm birth, <37 wk	23,618 (11.4)	2526 (14.8)	< .0001	1.25 (1.19–1.31)	1.17 (1.12–1.23)
Intrauterine fetal death	1148 (0.6)	110 (0.7)	.26	1.12 (0.92–1.38)	1.07 (0.87–1.32)

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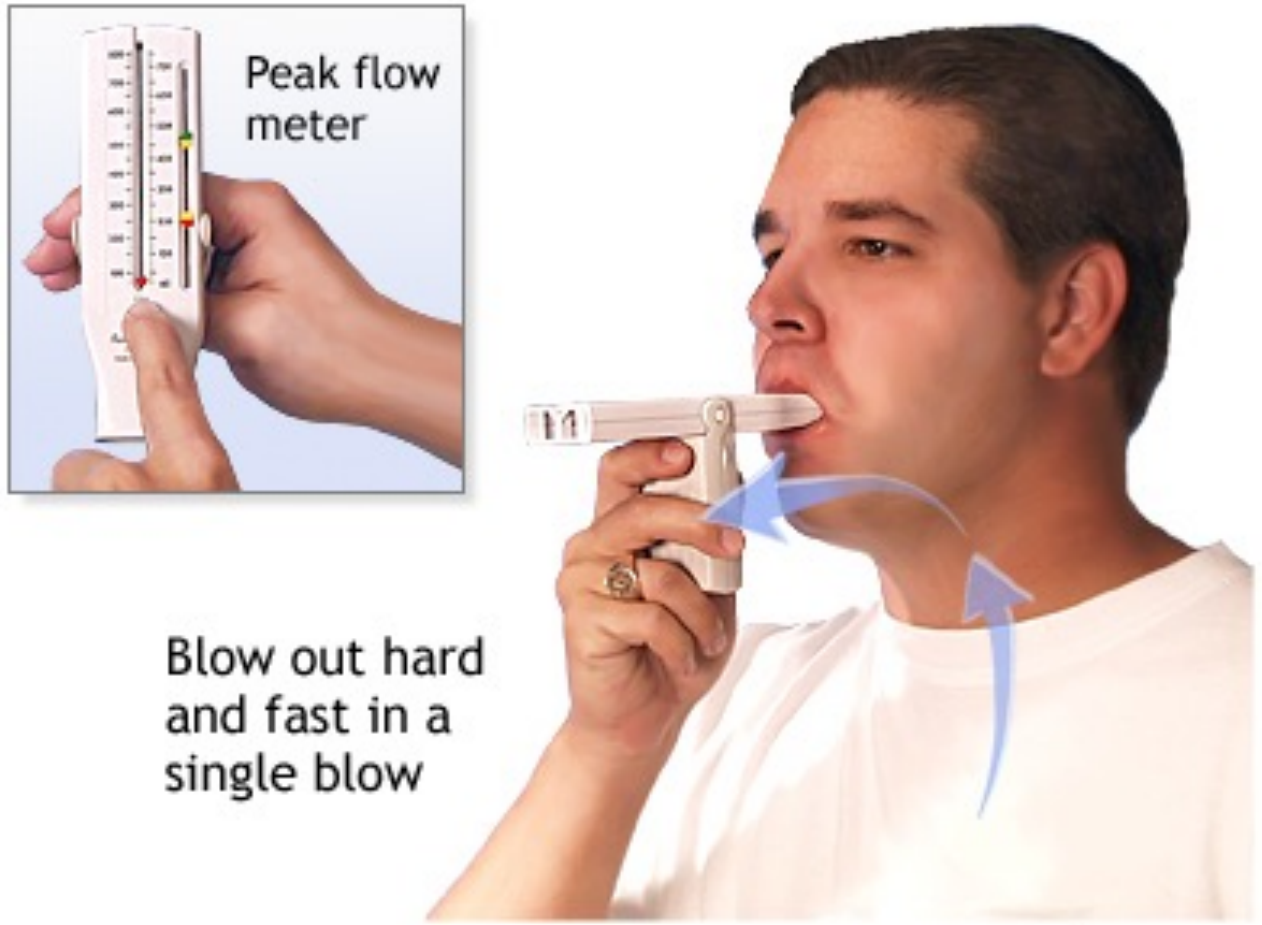
Asthma

Treatment

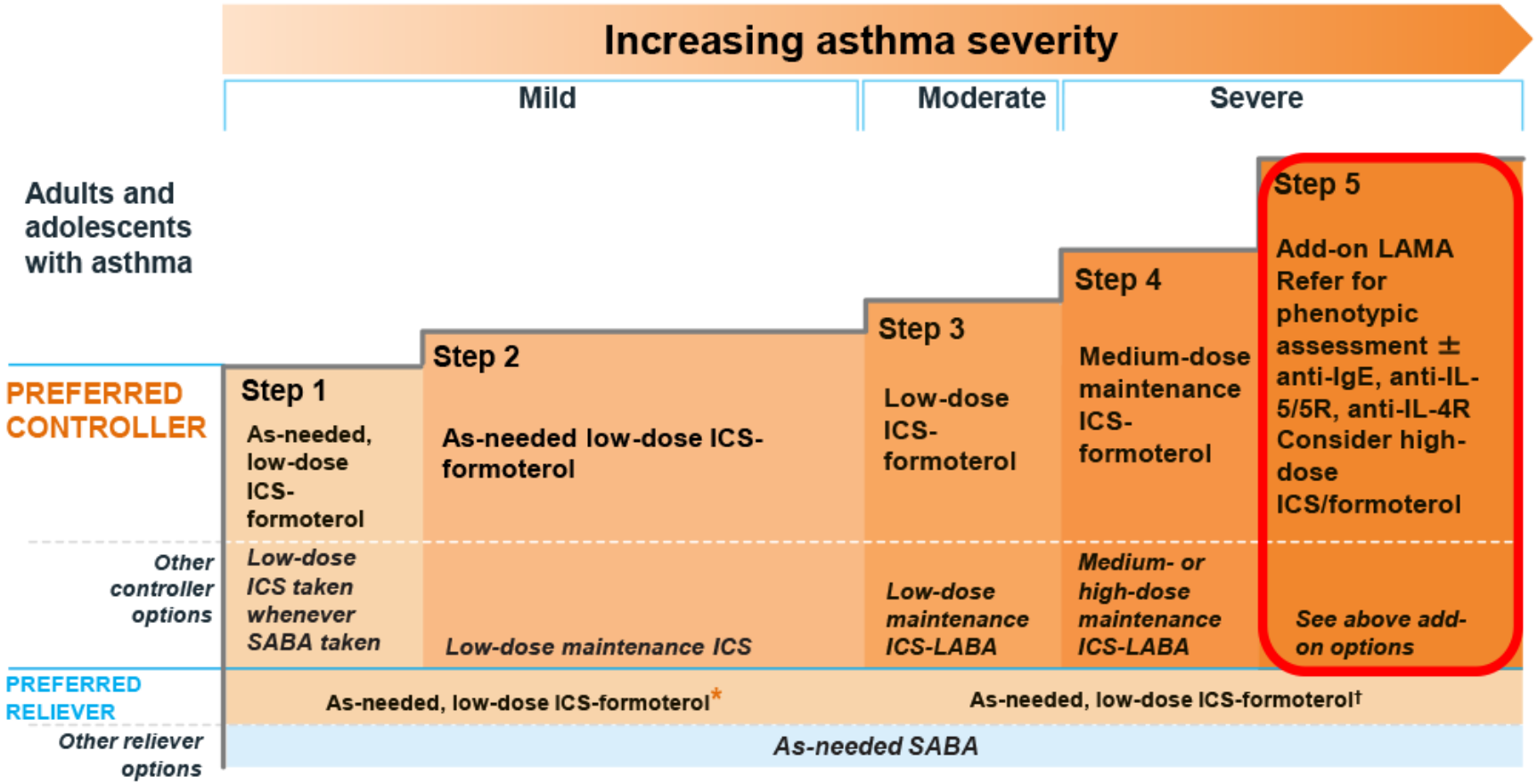
- Avoiding triggers
- Continuing prepregnancy meds
  - Known decrease in Rx fills in the first trimester
- Establish a baseline
  - FEV1 requires PFTs
  - PEFR (peak flows) do not
    - Establish a PEFR when healthy
    - Green zone >80%
    - Yellow zone 50-80%
    - Red zone <50%



Asthma

Chronic Pharmacotherapy

GINA 2021: Stepwise Treatment Approach



FDA = US Food and Drug Administration; ICS = inhaled corticosteroid; Ig = immunoglobulin; IL = interleukin; □LABA = long-acting β2-agonist; LTRA = leukotriene receptor antagonist; OCS = oral corticosteroid; SABA = short-acting β2-agonist.

Adapted from GINA. Global Strategy for Asthma Management and Prevention. Updated 2021 (https://ginasthma.org/wp-content/uploads/2021/05/GINA-Main-Report-2021-V2-WMS.pdf). Accessed 7/25/21.

Medication	Low dose	Medium dose	High dose
ICS-SABA combination			
Budesonide-albuterol HFA (Brand name: Airsupra)*			
NOTE: Not used for maintenance therapy. Acute symptom relief: Budesonide-albuterol (80 mcg/90 mcg) 2 inhalations as needed (usual maximum: 12 inhalations/day).			
ICS-LABA combinations			
Beclomethasone [beclometasone]-formoterol DPI or HFA (Not available in United States or Canada, but available elsewhere [sample brand names: Formodual, Fostair, Foster])¶ Δ			
100 mcg/6 mcg	1 inhalation twice a day	2 inhalations twice a day	
200 mcg/6 mcg			2 inhalations twice a day
Budesonide-formoterol HFA (Brand names: Symbicort, Breyna)¶			
80 mcg/4.5 mcg	2 inhalations twice a day		
160 mcg/4.5 mcg		2 inhalations twice a day	
Fluticasone furoate-vilanterol DPI (Brand name: Breo Ellipta)Δ			
NOTE: Inhaled fluticasone furoate has a greater anti-inflammatory potency per microgram than fluticasone propionate inhalers. Thus, fluticasone furoate is administered at a lower daily dose and used only **once** daily.			
50 mcg/25 mcg◇	1 inhalation once daily		
100 mcg/25 mcg		1 inhalation once daily	
200 mcg/25 mcg			1 inhalation once daily
Fluticasone propionate-formoterol MDI (Not available in United States or Canada, but available elsewhere [sample brand name: Flutiform])			
50 mcg/5 mcg	2 inhalations twice daily		
125 mcg/5 mcg		2 inhalations twice daily	
250 mcg/10 mcg			2 inhalations twice daily
Fluticasone propionate-salmeterol DPI (Brand names: Advair Diskus, Wixela Inhub)Δ			
100 mcg/50 mcg	1 inhalation twice a day		
250 mcg/50 mcg		1 inhalation twice a day	
500 mcg/50 mcg			1 inhalation twice a day
Fluticasone propionate-salmeterol HFA (Brand name: Advair HFA)			
45 mcg/21 mcg	2 inhalations twice a day		
115 mcg/21 mcg		2 inhalations twice a day	
230 mcg/21 mcg			2 inhalations twice a day

Asthma

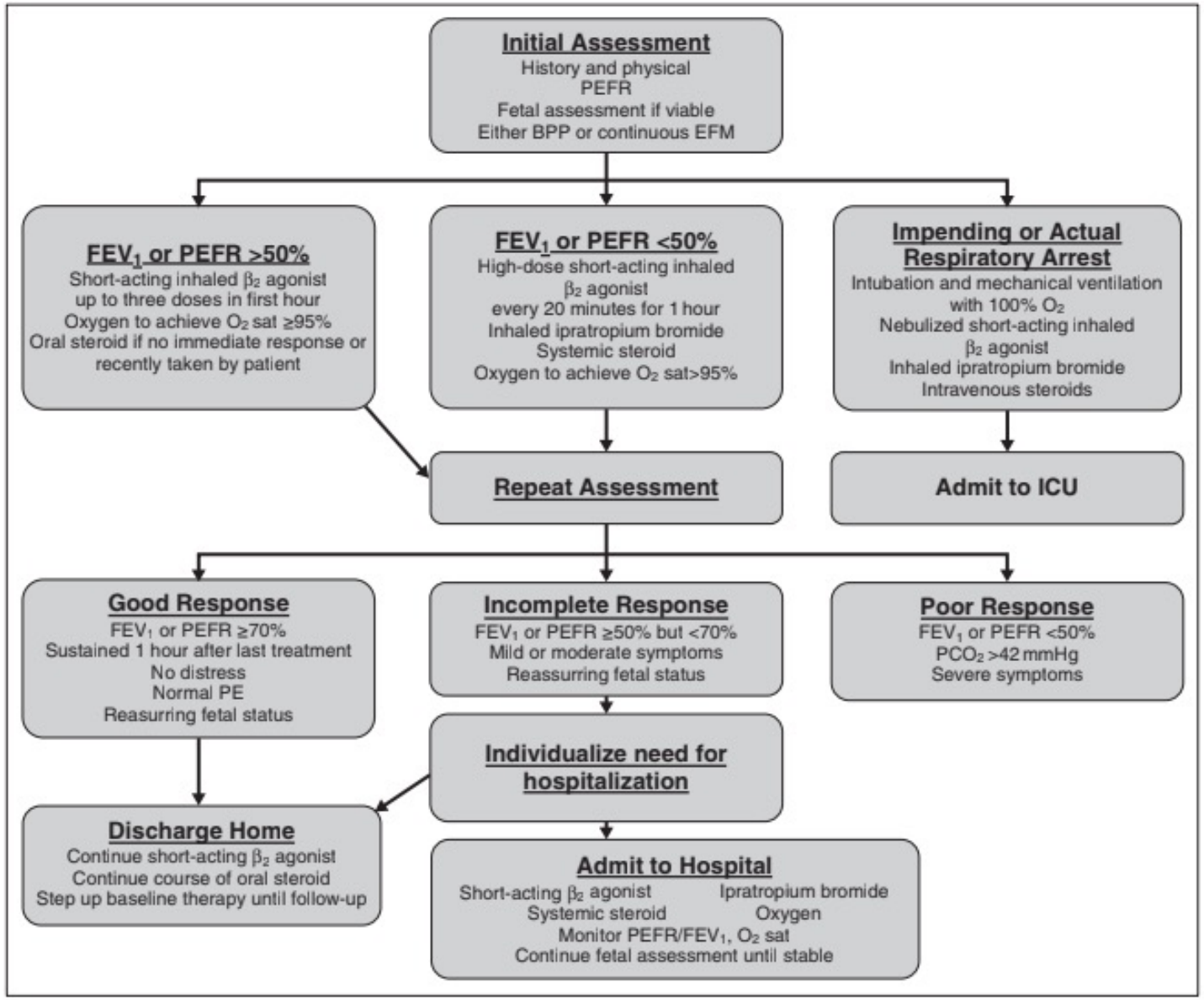
Less common meds in pregnancy

- Theophylline
  - Phosphodiesterase and adenosine receptor blocker
  - Lots of side effects
  - Requires blood level monitoring
- Leukotriene modulators (motelukast)
  - Blocks leukotrienes from causing bronchospasm
  - Used in aspirin mediated bronchospasm
  - Probably safe in pregnancy
- Omalizumab
  - Monoclonal antibody against IgE
  - No observed harm in limited data

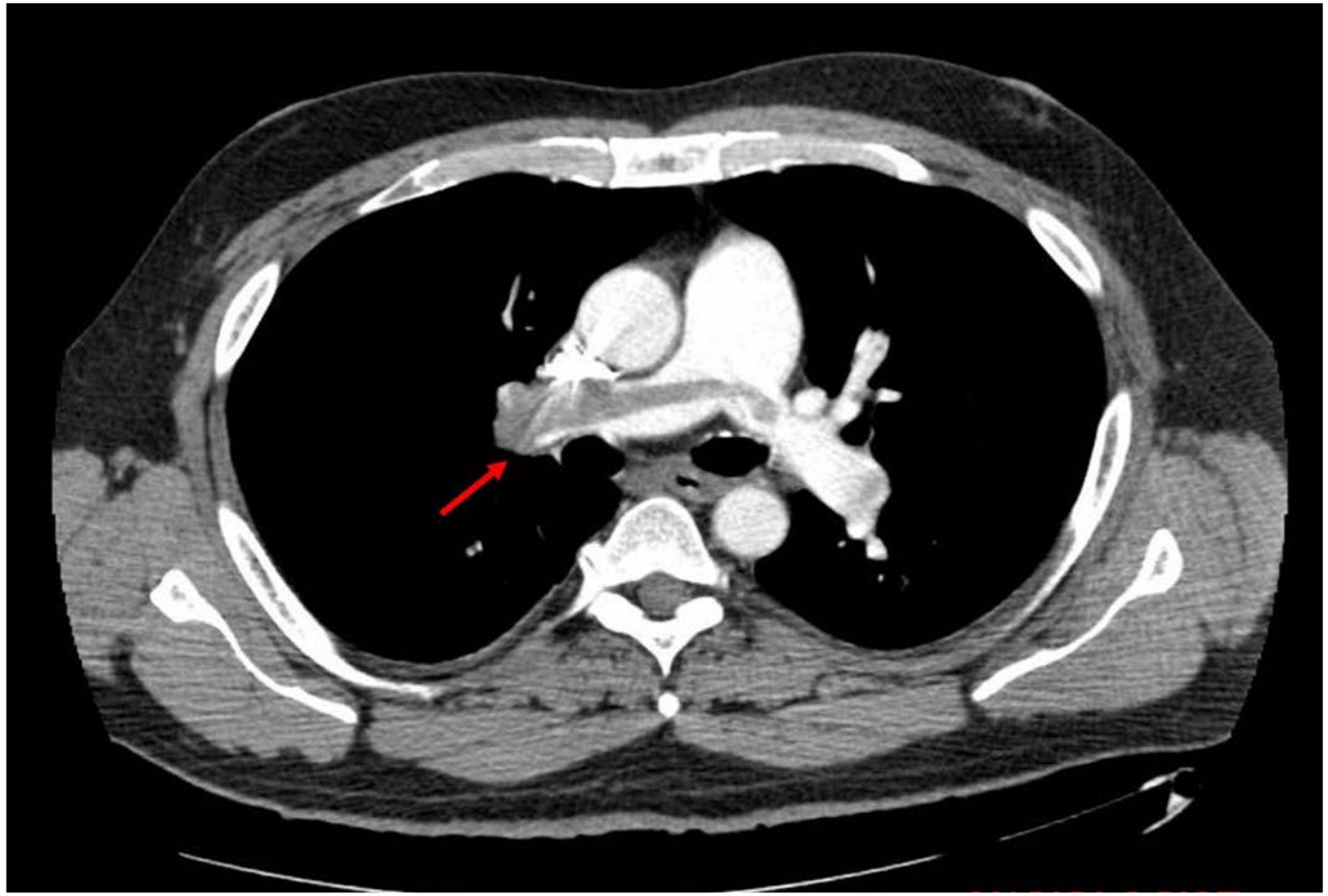
Asthma

Treating an acute exacerbation

- Alterations to typical asthma care:
  - Consider fetal monitoring
  - Higher SpO2 goals
  - Lower CO2 threshold
  - Less reserve



Pulmonary embolism



Pulmonary embolism

Epidemiology

- 6th leading cause for maternal mortality in U.S.
- 10-30% of maternal deaths
- Absolute incidence 0.1%
- 14% increase in VTE-associated pregnancy hospitalizations 1994-2009

Pulmonary embolism

Presentation

- Ranges from asymptomatic to sudden death
- Overlap with normal physiologic symptoms of pregnancy
- Small case series of 38 patients
  - 62% dyspnea
  - 55% pleuritic chest pain
  - 24% cough
  - 18% sweating

Pulmonary embolism

Workup

- Arterial blood gases not useful
  - 59% patients with normal a-a gradient
- D-dimer not typically used
  - Lack of normal reference in pregnancy
  - Sensitivity of 73%: so not too useful when negative
- Well's criteria not useful
  - High prevalence of tachycardia

ORIGINAL ARTICLE

Pregnancy-Adapted YEARS Algorithm for Diagnosis of Suspected Pulmonary Embolism

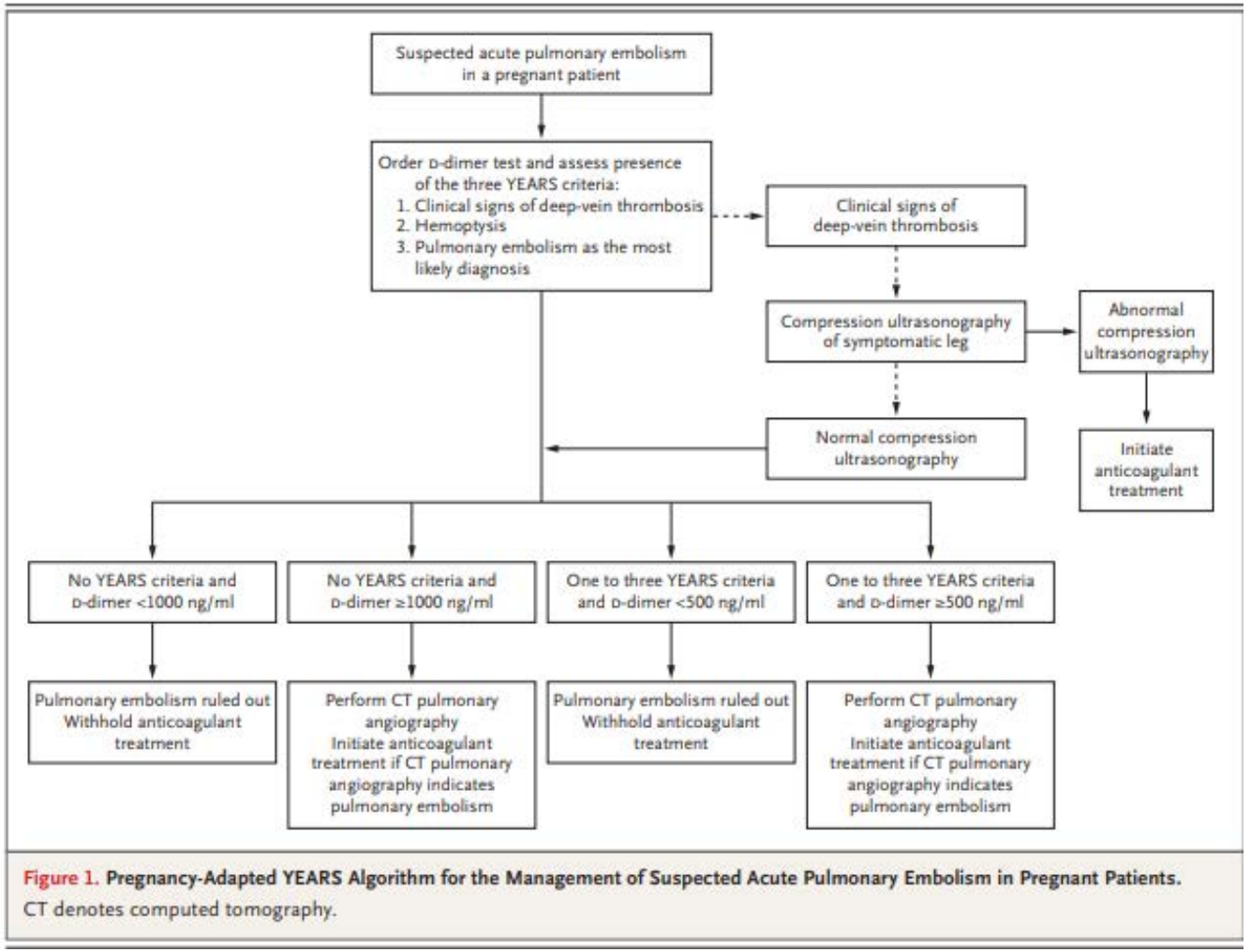


Figure 1. Pregnancy-Adapted YEARS Algorithm for the Management of Suspected Acute Pulmonary Embolism in Pregnant Patients.
CT denotes computed tomography.

Pulmonary embolism

Workup

- VQ scan: test of choice with normal CXR
  - High rate of indeterminate scans in general population
    - Due to CXR anomalies
  - 75-93% diagnostic VQ scans in pregnancy
  - "Normal:" 0-6% chance of PE
  - "High:" 56-96% chance of PE
- CT pulmonary angiography
  - High negative predictive value in pregnancy
  - BUT, up to 30% nondiagnostic in pregnancy (U-King-Im, 2008)
  - Consider when VQ scan not available or indeterminate
  - Is comparable or inferior to VQ scan in pregnancy

Diagnosing Pulmonary Embolism in Pregnancy Using Computed-Tomographic Angiography or Ventilation–Perfusion

Alison G. Cahill, MD, MSCI, Molly J. Stout, MD, George A. Macones, MD, MSCE, and Sanjeev Bhalla, MD

Pulmonary embolism

Radiation exposure

- What is the radiation risk?
  - CTPA has lower fetal radiation than VQ
    0.003-0.131 mGy vs 0.32-0.74 mGy
  - CTPA has higher maternal radiation than VQ
    - 7.3 vs 0.9 mSv
  - VQ delivers 150-fold lower breast/lung radiation
  - CXR + VQ scan + CTPA is still less than 0.5 rad

Table 1:
Potential Health Effects (Other Than Cancer) of Prenatal Radiation Exposure

Acute Radiation Dose* to the Embryo/Fetus	**Time Post Conception** Up to 2 weeks	**Time Post Conception** 3rd to 5th weeks	**Time Post Conception** 6th to 13th weeks	**Time Post Conception** 14th to 23rd weeks	**Time Post Conception** 24th week to term
< 0.10 Gy (10 rads)†	Non-cancer health effects NOT detectable				
0.10–0.50 Gy (10–50 rads)	Failure to implant may increase slightly, but surviving embryos will probably have no significant (non-cancer) health effects.	Growth restriction possible	Growth restriction possible	Non-cancer health effects unlikely	
> 0.50 Gy (50 rads) The expectant mother may be experiencing acute radiation syndrome in this range, depending on her whole-body dose.	Failure to implant will likely be high, depending on dose, but surviving embryos will probably have no significant (non-cancer) health effects.	Probability of miscarriage may increase, depending on dose. Probability of major malformations, such as neurological and motor deficiencies, increases. Growth restriction is likely	Probability of miscarriage may increase, depending on dose. Growth restriction is likely.	Probability of miscarriage may increase, depending on dose. Growth restriction is possible, depending on dose. (Less likely than during the 6th to 13th weeks post conception) Probability of major malformations may increase	Miscarriage and neonatal death may occur, depending on dose.

Pulmonary embolism

Treatment

- Therapeutic anticoagulation
  - Lovenox > heparin gtt
- Suction thrombectomy?
- Catheter directed lytics?
- Systemic lytics?
  - Complication rate similar to non-pregnant population: 1% mortality, 8% maternal hemorrhage
  - PPH risk highest if used within 8 hours of delivery
  - 6% fetal loss rate possibly causal by thrombolytic therapy
  - No issues in liveborn children

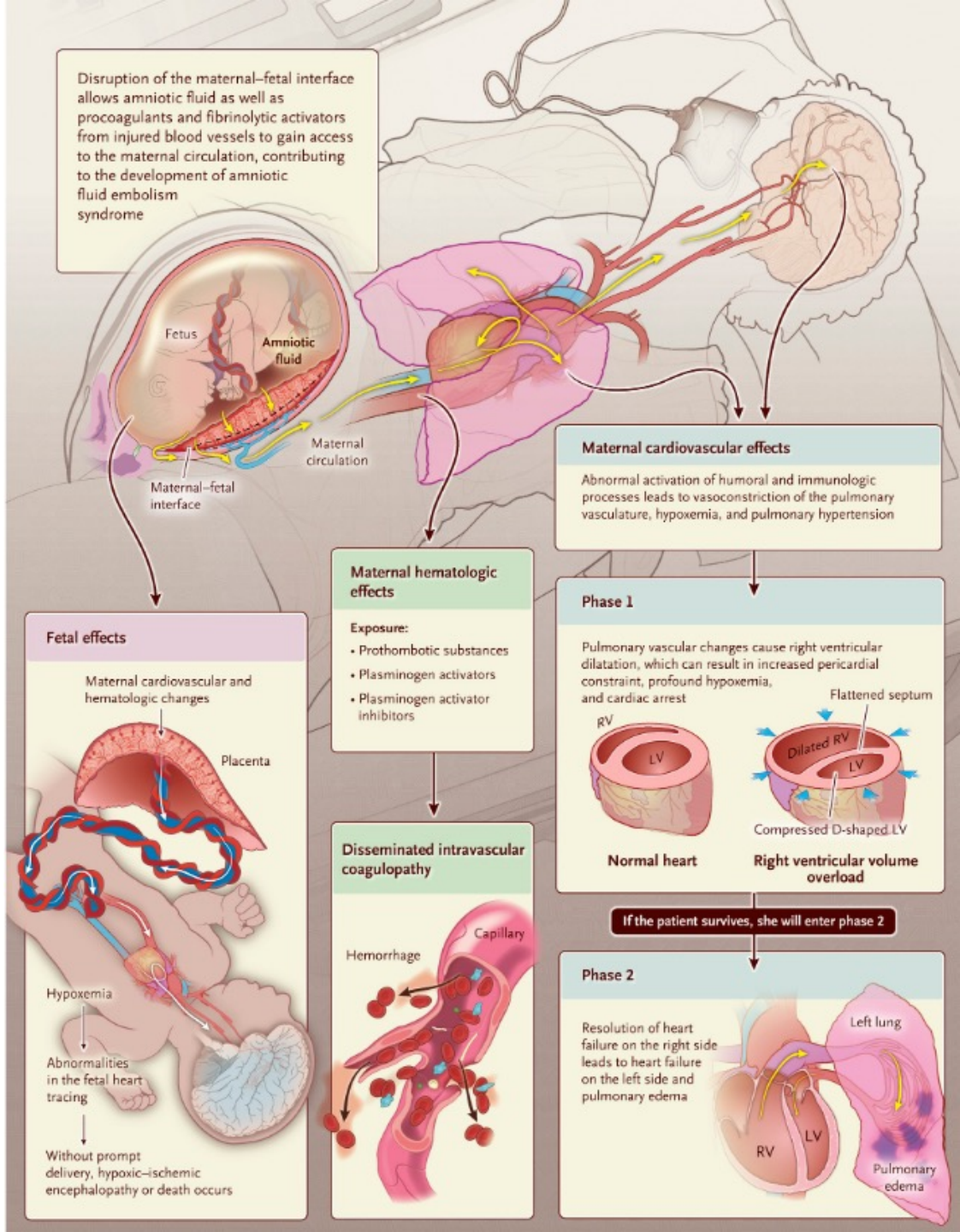
American Heart Association Definitions of Massive, Submassive, and Low-Risk PE and Associated Mortality

PE Classification	Definition	Mortality
Massive	Acute PE with sustained hypotension (< 90 mm Hg systolic) > 15 minutes or requiring inotropic support	25%–65% (62)
Submassive	Systolic pressure > 90 mm Hg and either: (a) RV dysfunction (CT, BNP/proBNP, ECG changes) or (b) myocardial necrosis (elevated troponins)	3% (20)
Low risk	Absence of hypotension, RV dysfunction, and myocardial necrosis	<1% (20)

Note.—BNP = brain natriuretic peptide, ECG = electrocardiography.

Amniotic fluid embolism

- 1:16,000 to 1:50,000 deliveries
- Disruption of maternal fetal interface
- Most commonly at the time of delivery
- Bad luck->bad heart-> bad blood
  - Acute pulm vasoconstriction
  - Acute RV failure-> arrest (87%)-> LV failure
  - Prothrombotic substance-> DIC
- 20-60% mortality
  - 60% of survivors have neurologic impacts



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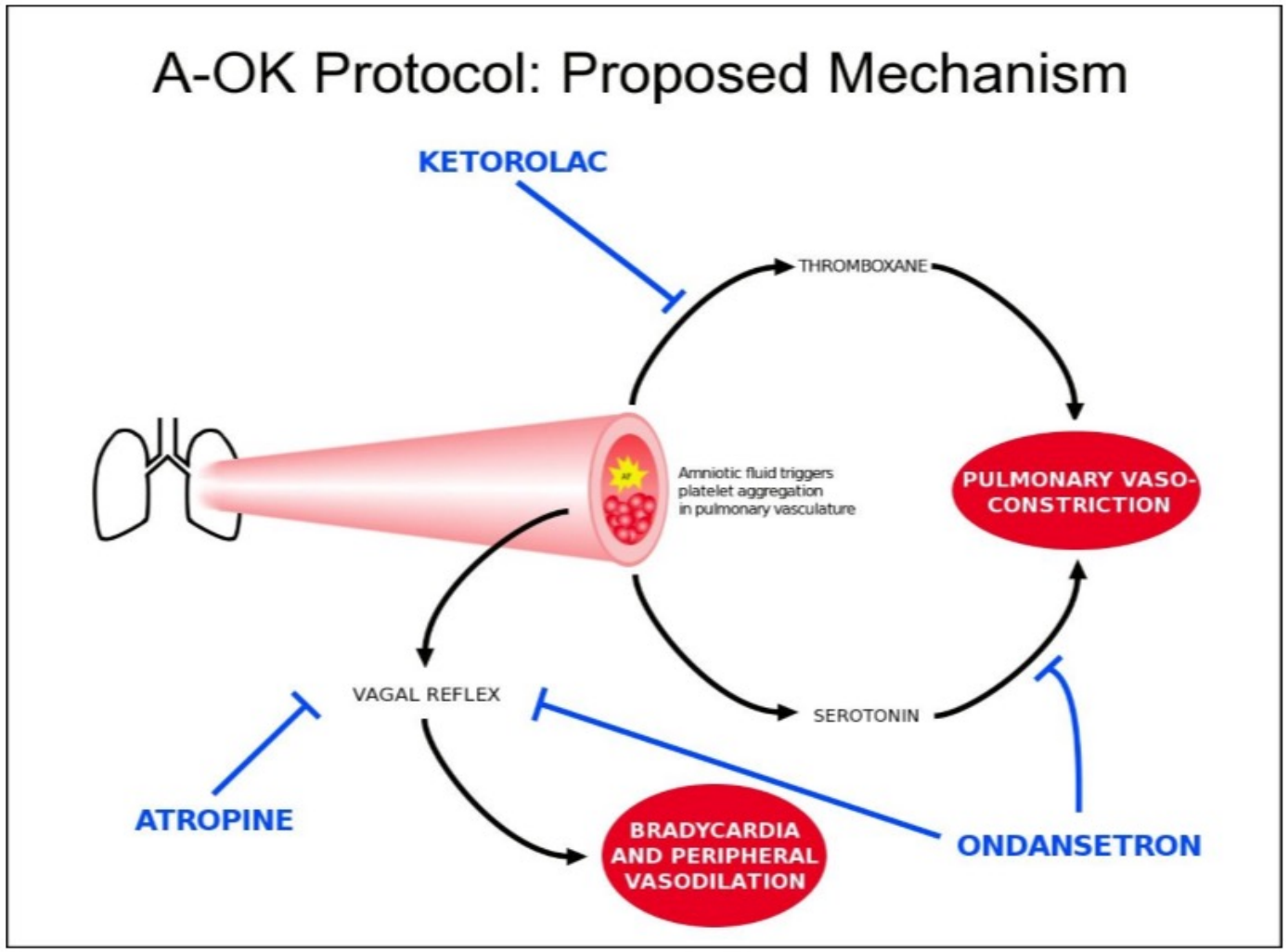
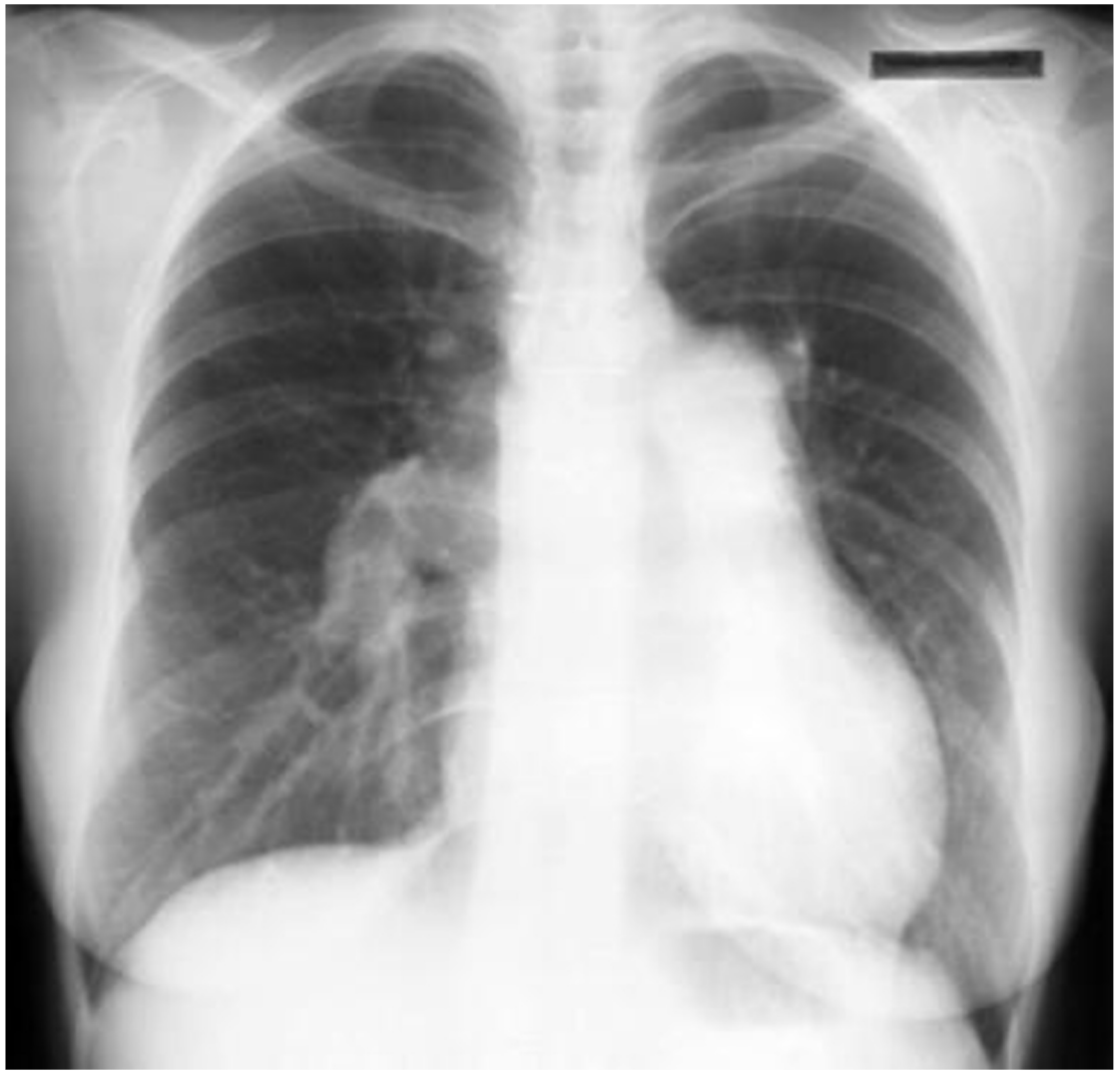
AFE treatment

- Supportive care
  - ACLS
  - ECMO
- A-OK protocol
  - Atropine
  - Ondansetron
  - ketorolac



Pulmonary Hypertension



Pulmonary Hypertension

- Heterogenous group of diseases (Hemnes, 2015)
  - Characterized by mPAP ≥25 mmHg
  - May be accompanied by increase of pulmonary vascular resistance
  - WHO classification

Pulmonary Hypertension

Table 1.

Table 1. Updated clinical classification of pulmonary hypertension (PH)

View table image

Group	Definition	Selected etiologies
Group 1	Pulmonary arterial hypertension (PAH)	Idiopathic PAH, connective tissue disease–associated PAH, congenital heart disease–associated PAH, heritable PAH, schistosomiasis-associated PAH, persistent PH of the newborn
Group 2	PH due to left heart disease	Left ventricular systolic dysfunction, left ventricular diastolic dysfunction, aortic or mitral valvular heart disease
Group 3	PH due to lung diseases and/or hypoxia	Chronic obstructive pulmonary disease, interstitial lung disease, sleep-disordered breathing, developmental lung disease
Group 4	Chronic thromboembolic PH	
Group 5	PH with unclear multifactorial mechanisms	Sarcoidosis, chronic hemolytic anemia

Note Adapted from Simonneau et al.[1]

Pulmonary Hypertension

- Improved outcomes in modern era, but mortality remains high (Hemnes, 2015)
  - 30-56% in older studies
  - 16-22% in recent studies
    - Subject to publication bias, availability of termination
  - Rapid deterioration occurs 20-24 weeks GA
  - Usually due to RV failure

Pulmonary Hypertension

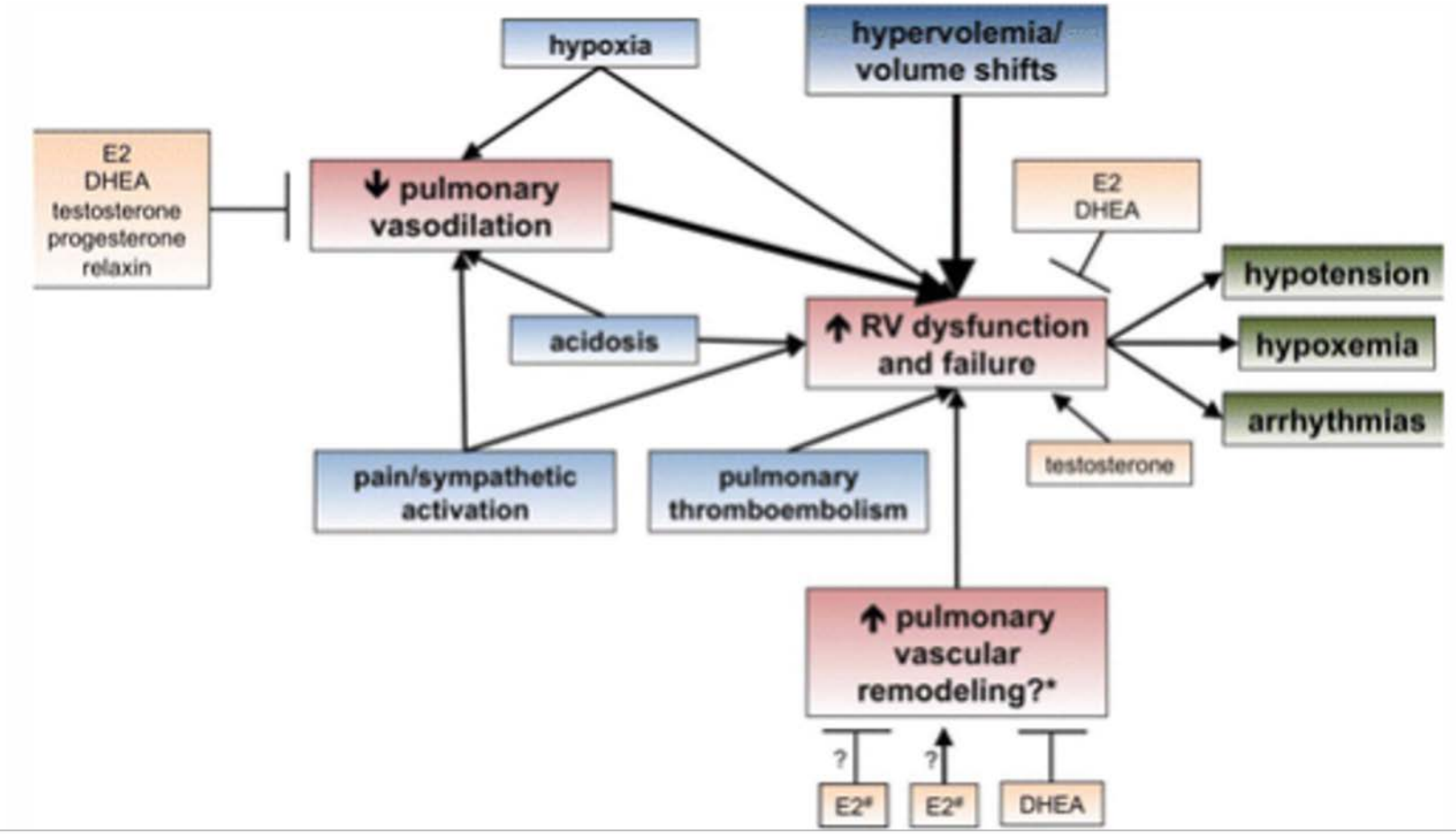


Figure 3. Pathophysiology of pulmonary hypertension (PH) and right ventricular (RV) dysfunction in pregnancy. Items in red represent the underlying preexisting alterations in PH; items in blue represent pregnancy-related modifiers that may aggravate these alterations. Potential contributions of sex hormones are shown in yellow (derived from studies in normal animals as well as PH models). Decreased pulmonary

Pulmonary Hypertension

Figure 2. Adaptation of the pulmonary vascular system and the right ventricle (RV) to increased pulmonary blood flow during pregnancy in a healthy patient and in pulmonary vascular disease. Note that the diseased pulmonary vasculature in pulmonary arterial hypertension (PAH; characterized by vasoconstriction, pulmonary vascular remodeling with lumen obliteration, and in situ thrombosis) is unable to accommodate the increased cardiac output, thus leading to RV strain, dilation, and eventually decompensation. PE: pulmonary embolism.

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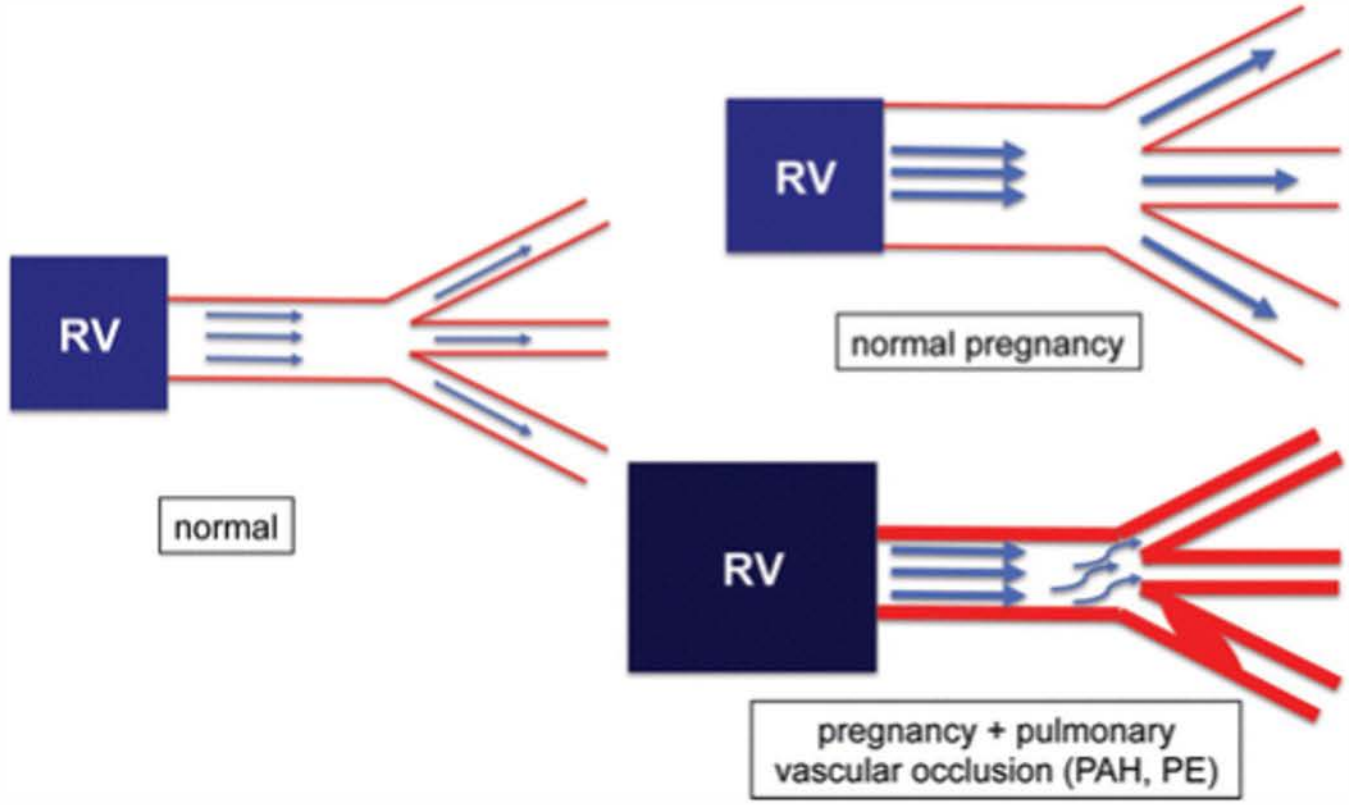

Pulmonary Hypertension

- All patients should be counseled to avoid pregnancy (Hemnes, 2015)
  - Especially with pulmonary arterial hypertension
- Permanent contraception should be strongly considered in pregnancy
  - Hysteroscopic sterilization or laparoscopic BTL
  - Progestin-only is second-line
  - Estrogen contraindicated

Pulmonary Hypertension

- Well, she's pregnant.

Pulmonary Hypertension

- Well, she's pregnant.
- Now what?

Pulmonary Hypertension

- Genetic counseling (Hemnes, 2015)
  - Should be offered to all patients with idiopathic or hereditary PH
  - BMPR2 mutations in 80% of families
    - Other mutations also known (CAV1, KCNK3, EIF2AK4)
  - Dominant gene with weak penetrance
    - Only 20% will develop clinical PH

Pulmonary Hypertension

- Pregnancy management (Hemnes, 2015)
  - Counsel and offer termination
  - Multidisciplinary Team
    - MFM, pulmonary hypertension specialist, cardiologist, anesthesiologist, neonatologist
  - Highest risk period is peripartum and up to 2 months postpartum
  - Cesarean section recommended over VD
  - Epidrual or spinal recommended over general
  - Avoid vasalvagal triggers

Pulmonary Hypertension

- Medications (Hemnes, 2015)
  - Prostaglandins are potent pulmonary vasodilators and recommended in RV impairment
    - Epoprostenol, treprostinil, and iloprost
  - Phosphodiesterase 5 inhibitors
    - Experience with sildenafil + prostaglandin in pregnancy
    - Monotherapy reserved for normal RV function
  - Calcium channel blockers
    - Improved prognosis if used in patients who respond to inhaled vasodilator
  - Endothelin receptor antagonists
    - Ambrisentan, bosentan, macitentan, and sitaxentan
    - Category X

Pulmonary Hypertension

Figure 4. Recommended evaluation of and follow-up for a pregnant patient with pulmonary arterial hype
natriuretic peptide; ETRA: endothelin receptor antagonist; FC: World Health Organization function class; I
low-molecular-weight heparin; PH: pulmonary hypertension; RV: right ventricular; 6MWT: 6-minute walk

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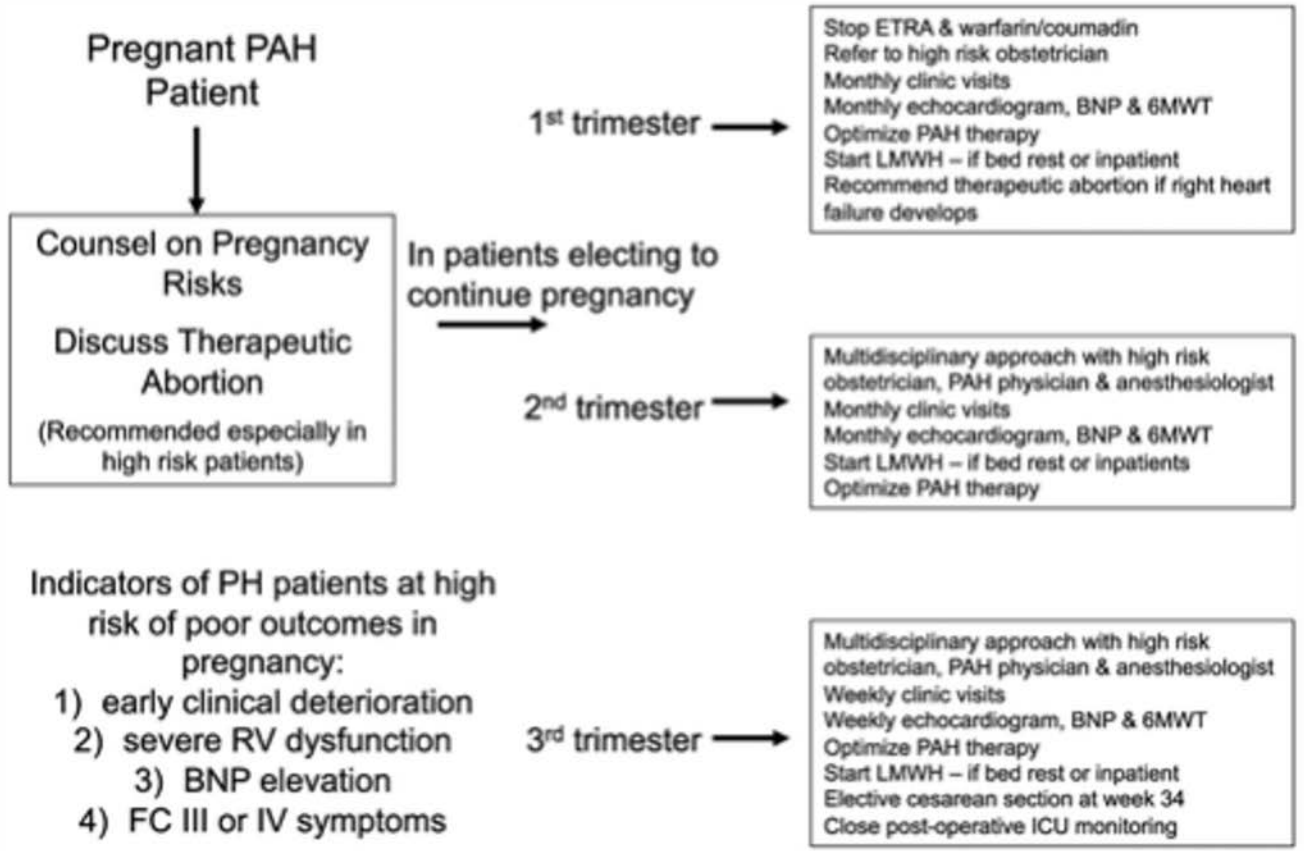
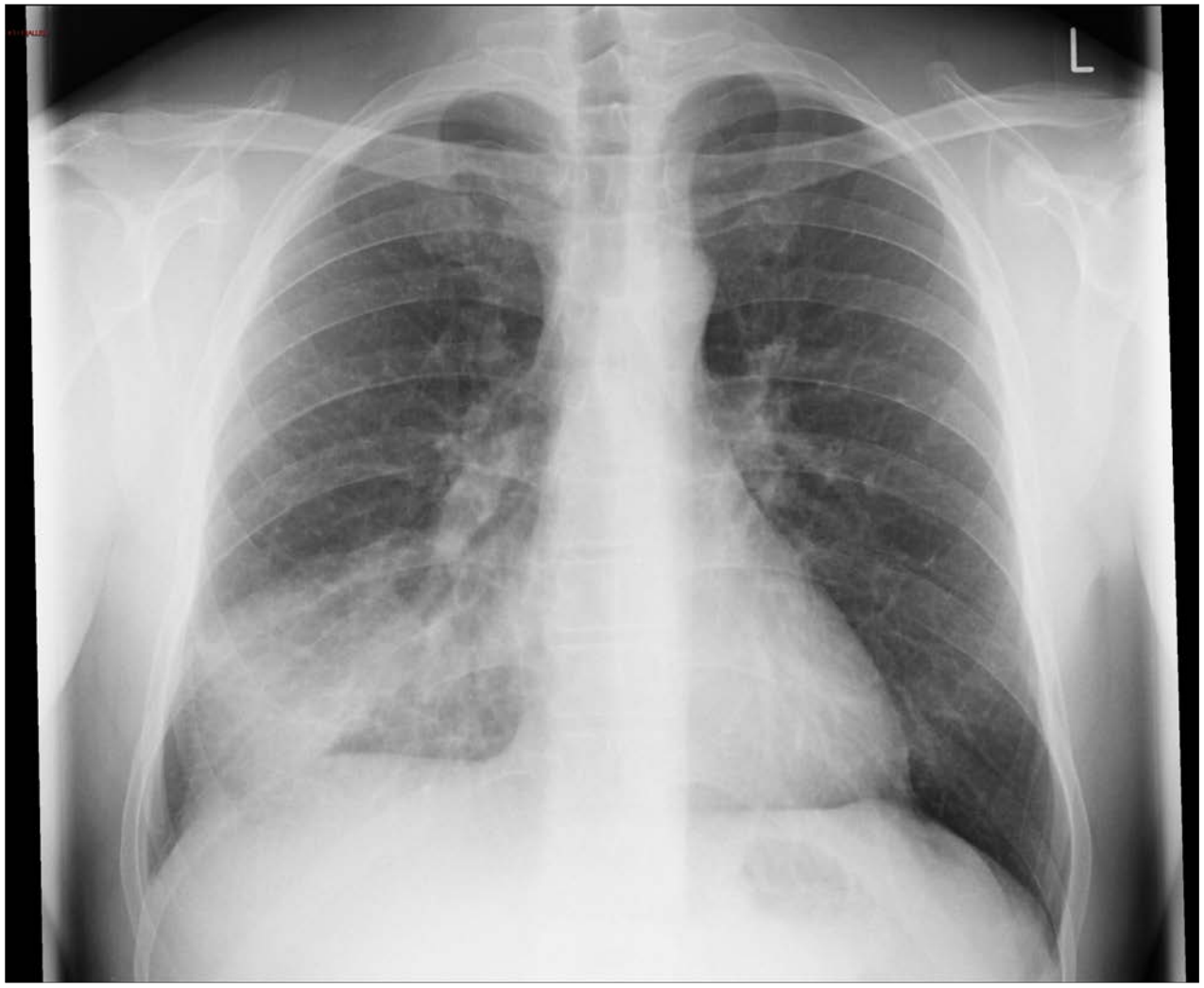


Pulmonary Hypertension

- Delivery management (Hemnes, 2015)
  - Consider IV prostaglandins
  - Central venous catheter, arterial line
  - Swan-Ganz catheterization not recommended
  - Prophylactic heparin recommended

Pneumonia



Pneumonia

- 1.2-2.7 per 1,000 deliveries, 0-4% mortality (Lim 2001)
  - Not significantly different from nonpregnant
- Associated with:
  - Preterm <34 week delivery (34%)
  - LBW (16%)
- No clear evidence on perinatal mortality

Pneumonia

- Risk factors (Lim 2001)
  - Asthma
  - Tocolysis
  - Smoking
  - ?Steroids for fetal lung maturity
  - Underlying lung disease
- Misdiagnosis common in pregnancy
    - Up to 20%
    - Leading misdiagnosis: pyelenephritis, appendicitis, PTL
- Diagnosis by CXR

Pneumonia

- Pathogens (Lim 2010)
  - Bacterial
    - –S. pneuomoniae and H. influenzae
    - –Legionella and mycoplasma rare
      - »Publication bias?
    - –Coxiella burnetti (Q fever)
      - »Contact with newborn animals
      - »Poor fetal outcome
        - 15 case series: 10 SABs, 3 PTD, 2 normal

Pneumonia

- Pathogens
  - Influenza virus (Jamieson 2009)
    - H1N1 epidemic in 2009
    - Pregnant women not more susceptible, but more severely affected
      - 1% general population mortality, 5% in pregnancy
      - Severe morbidity in 3T and 4 weeks postpartum
    - Fetal anomalies associated with fever in 1T
      - Cleft lip, ONTD, hydrocephlay, cardiac anomalies
      - Attenuated with use of anti-pyretic
    - Also associated with poor obstetrical outcome
      - SAB, PTD, IUGR, IUFD

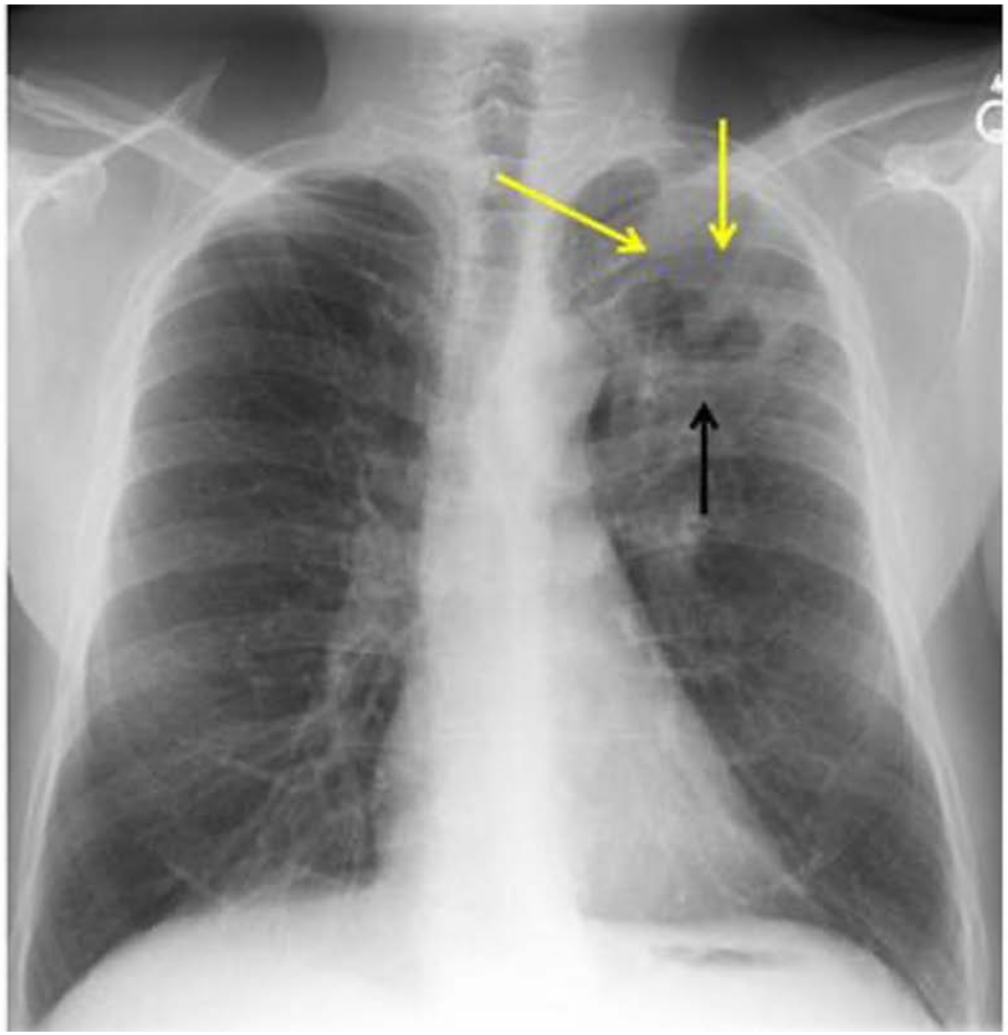
Pneumonia

- Pathogens
  - Varicella virus (Lim 2010)
    - 5-10 per 10,000 pregnancies
    - Pneumonia occurs in 15-20% of pregnant women
    - Mortality as high as 35%
    - Most severe in 3T
    - 2% risk of fetal infection prior to 20 weeks
      - » LBW, scarring of legs/arms/CNS/eyes

Pneumonia

- Pathogens (Lim 2010)
  - Fungal
    - Rare in pregnancy
    - Coccidioidomycosis
      - 10 cases over 6 years
      - Greater risk for dissemination
      - High mortality if aquired in 3T
    - Cryptococcas
      - Rare in immunocompetent individuals
      - 5 cases reported
        - » Cough/dyspnea to severe pleuritic chest pain
        - » No reported deats
      - Blastomycosis
        - » Rare, unclear impact by or on pregnancy

Tuberculosis



Tuberculosis

- Background (Sugarman 2014)
  - More than 200,000 cases of TB in pregnancy worldwide in 2011
  - Pathogenesis similar to nonpregnant popluation
  - Morbidity reflection of general incidence

Tuberculosis

- Diagnosis (Laibl 2005)
  - Routine testing in pregnant women not indicated!
  - Only if indication for treatment
    - Active disease
    - Immunocompromised and at risk for latent TB
  - In absence of this, targeted testing and treatment should be delayed to 3 months postpartum

Tuberculosis

- Testing (Worjohloh 2011)
  - Skin test
  - Interferon gamma release assays
  - Both are safe in and not influenced by pregnancy
- If positive, screen for active disease
  - History
  - Physical
  - CXR

Tuberculosis

Treatment (American Thoracic Society, 2003)

- Latent TB
  - Only if high risk for progression to active disease
  - Daily Isoniazid x 9 months
  - 6-month duration and/or twice weekly directly observed therapy
- Active TB
  - Isoniazid, rifampin, and ethambutol administered x 2 months, AND
  - Isoniazid and rifampin for 7 months
  - Pyrazinamide not absolutely necessary
    - Limited safety data
    - Standard in pregnancy by WHO regimen
    - Consider in complicated cases
  - Streptomycin, kanamycin, amikacin, capreomycin contraindicated
    - Interferes with CN VIII development congenital deafness, renal toxicity

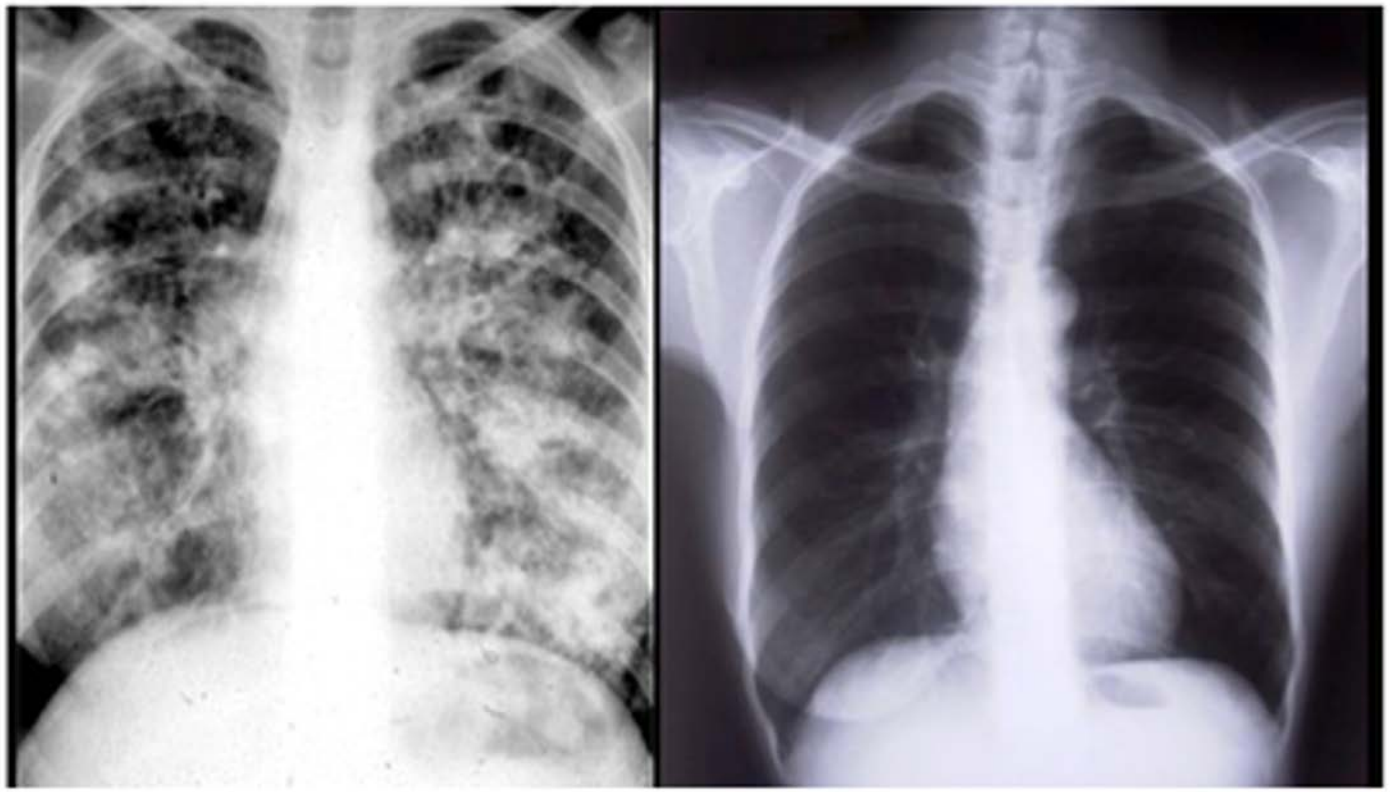
Tuberculosis

- Congenital TB is very rare (Manji 2001)
  - Associated with maternal HIV infection, miliary or uterine TB
  - In regions with high maternal HIV and TB rates
  - Hematogenous spread or fetal aspiration of AF
  - Respiratory distress, fever, hepatosplenomegaly, lethargy, LBW, low Apgars
  - Evaluate with neonatal CSF, placenta AFB stain/cx
  - Mortality of untreated congenital/neonatal TB is 50%

Tuberculosis

- Maternal-Infant separation (Manji 2001)
  - ONLY if mom has suspected active disease
  - Separation until mom is not infectious ONLY if mom has confirmed drug-resistance and newborn has no evidence of infection
  - Will always treat infant if mom has active disease
- Breastfeeding
  - Not contraindicated by disease or treatment
  - Supplemental pyridoxine for mother and infant

Cystic Fibrosis



Cystic Fibrosis Lung

Healthy Lung

Cystic Fibrosis

- Background (Patel, 2015)
  - Autosomal recessive disorder affecting 1 in 3,500 births
  - 2000 genes identified
  - 1/25 carrier rate in Caucasions
  - Disorder of cystic fibrosis transmembrane conductance regulator protein
    - Abnormal transport of chloride and sodium ions
    - Impaired clearance in respiratory, GI, and GU tracts
  - Respiratory failure, chronic infection, malabsorption, pancreatic insufficiency
    - Biliary tract cirrhosis, diabetes, male factor infertility
    - 20% develop diabetes by age 20

Cystic Fibrosis

- Background (Patel, 2015)
  - Median predicted survival 36.8 in women in 2011
  - Recent literature suggest normal female fertility
  - Pregnancy tolerated well with good-moderate lung function
    - FEV1 50-70%
    - However, treatments for CF increased during pregnancy

Cystic Fibrosis

- Increasing rates of delivery in women with CF (Patel, 2015)
  - 2.99 to 9.85 per 100,000 women from 2000-2010
  - 257 pregnancies reported in 2013 in the Cystic Fibrosis Foundation Registry 4 live births per 100 women

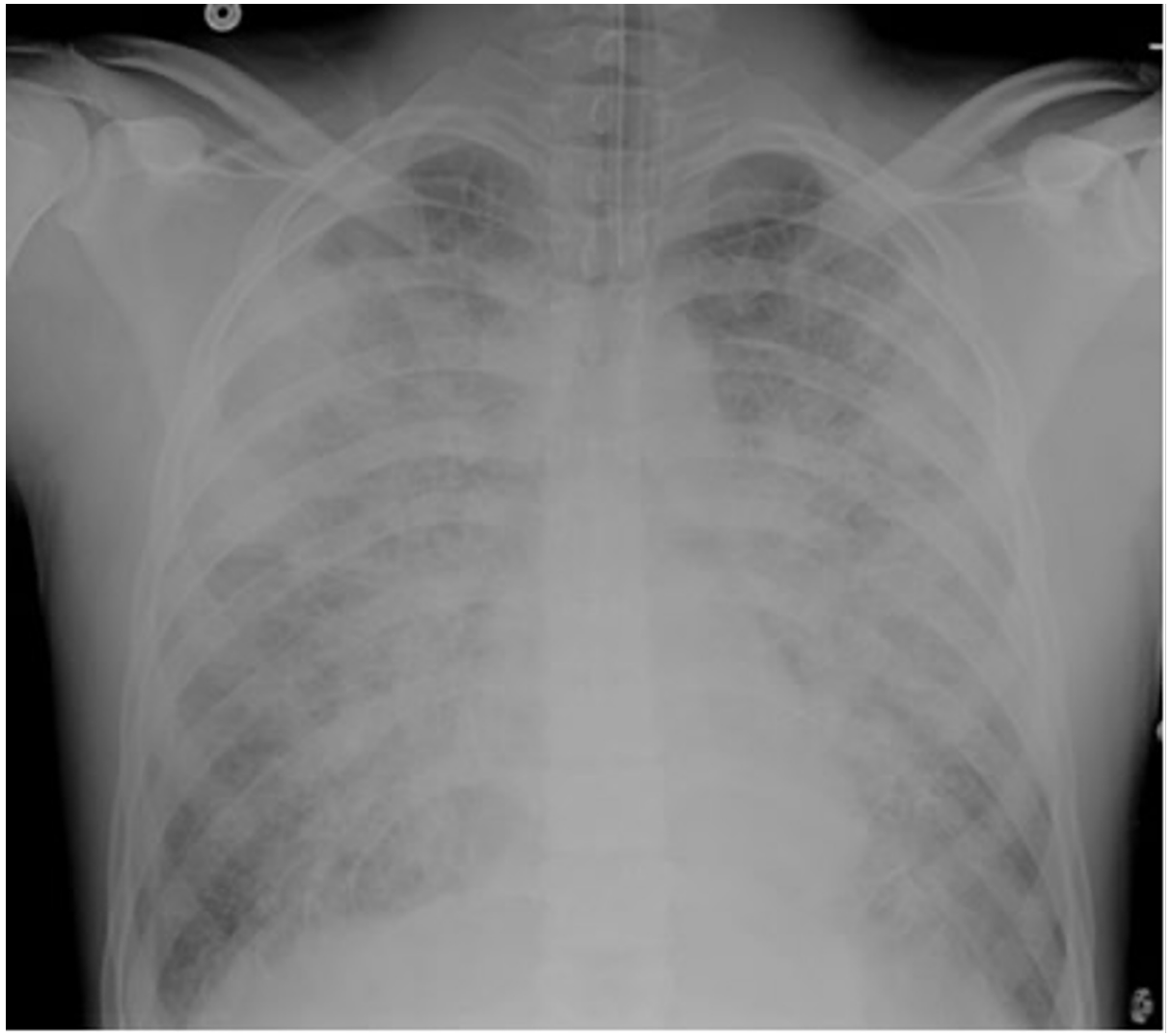
Cystic Fibrosis

- Higher risks of: (Patel, 2015)
  - Pneumonia (OR 69)
  - Mechanical ventilation (OR 32)
  - Death (OR 125)
  - Preterm labor (OR 2.5)
  - GDM (OR 2.5)
- Comparable risks of:
  - Cesarean, PIH, abruption, IUGR, PPH, chorioamnionitis
- Overall mortality: 1 percent
  - Worse with severe lung disease (pulmonary hypertension)

Cystic Fibrosis

- General guidelines: (Patel, 2015)
  - Achieving optimal pulmonary function prior to conception
  - Carefully monitoring during pregnancy
  - Providing genetic counseling
    - Carrier testing of the father
    - Options for prenatal diagnosis
  - Close monitoring of maternal nutrition, weight gain
  - Early screening for gestational diabetes

ARDS



ARDS

- Acute, diffuse inflammatory lung injury (Cole 2005)
- 16-70 per 100,000 in pregnancy
- Pathologic and Clinical hallmark:
  - Hypoxemia and bilateral opacities on CXR
  - Diffuse alveolar damage
- 30-50% mortality in obstetrical population
  - Long term morbidity
  - Similar to nonobstetrical population
  - 23-50% perinatal mortality and high rate of morbidity
    - Preterm labor, NRFHT

ARDS

- Berlin definition
  - Bilateral opacities without collapse or nodules
  - Respiratory collapse not explained by cardiac failure or pulmonary edema
  - Moderate to severe oxygenation impairment
    - Mild ARDS:
      - » PaO_2/FiO_2 >200 mmHg, but ≤300 mmHg, PEEP/CPAP ≥5 cm H_2O
    - Moderate ARDS:
      - » PaO_2/FiO_2 >100 mmHg, but ≤200 mmHg, PEEP ≥5 cm H_2O.
    - Severe ARDS:
      - » PaO_2/FiO_2 ≤100 , PEEP ≥5 cm H_2O

ARDS

- ARDS from obstetric and nonobstetric conditions (Cole 2005)
  - Amniotic fluid embolism
  - Chorioamnionitis
  - Trophoblastic embolism
  - Placental abruption
  - Aspiration
  - Pneumonia
  - Air embolism
  - Massive hemorrhage
  - Pyelonephritis

ARDS

- Risks of the obstetrical population: (Cole 2005)
  - Fluid administration and tocolytic therapy
  - Reduced albumin level and plasma oncotic pressure
    - Pulmonary edema develops at much lower pressures compared to nonpregnant patients

ARDS

- Adequate maternal oxygen saturation essential
  (Cole 2005)
  - General population: PaO2 55 mmHg, SaO2 88%
  - Pregnancy: PaO2 of 70 mm Hgm SaO2 95%

- Fetal CO2 clearance requires 10 mmHg gradient
  - PaCO2 of 45 mm Hg, maternal pH of 7.30 “seems reasonable”

ARDS

- Fetal assessment (Cole 2005)
  - EFM limited in critically ill patients
  - BPP potentially better modality
  - Soft recommendation of twice weekly testing at 26 wks or with change in maternal status

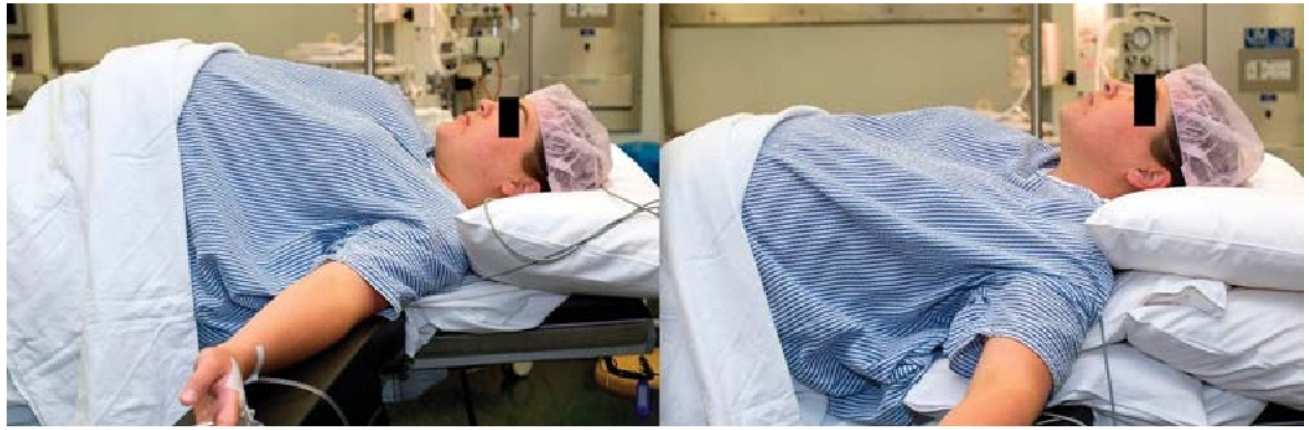
- No other major differences exist in the management
- Survival similar to ARDS in the general population
- Perimortem cesarean
  - Within 4 minutes for maternal and fetal benefit

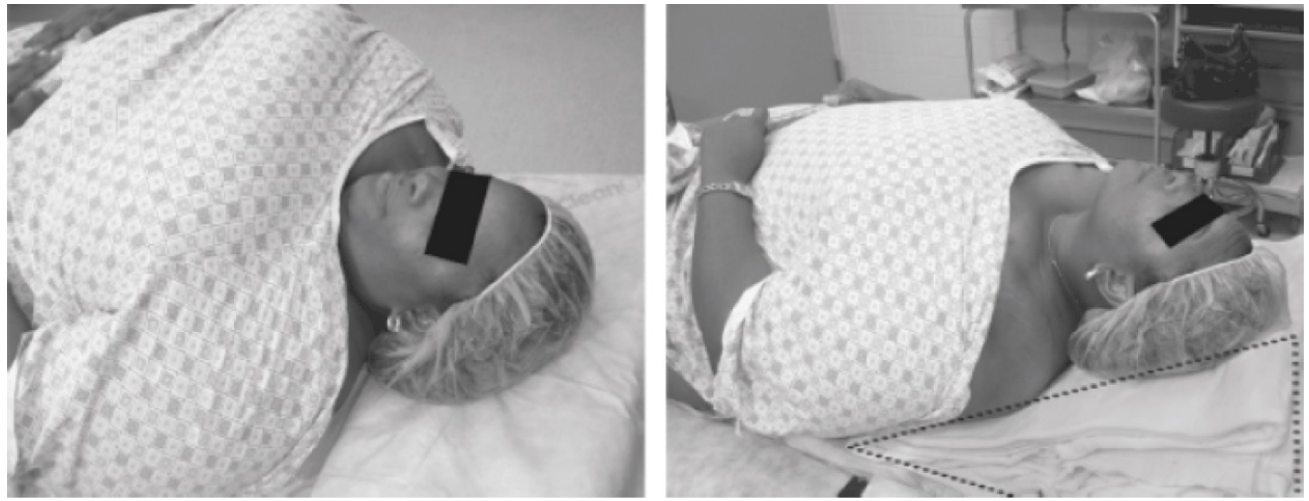
Acute respiratory failure

- The increased respiratory demands and decreased respiratory reserve
- Pregnancy related
  - Pulmonary edema
  - AFE
- Pregnancy associated
  - Viral ARDS
  - Asthma
  - Embolism

Indications for intubation	Indications for ventilation
• Need to secure airway • Depressed sensorium • Imperfect airway reflexes • Upper airway instability after trauma • Decreased airway patency • Need for sedation in a situation of poor airway control • Imaging (CT, MRT) and transportation of the patient	• Hypoxia: acute hypoxemic respiratory failure • Hypoventilation • Unacceptably high work of breathing • Hemodynamic compromise • Cardiorespiratory arrest • Refractory shock • Raised intracranial pressure • Flail chest

Intubation in Pregnancy

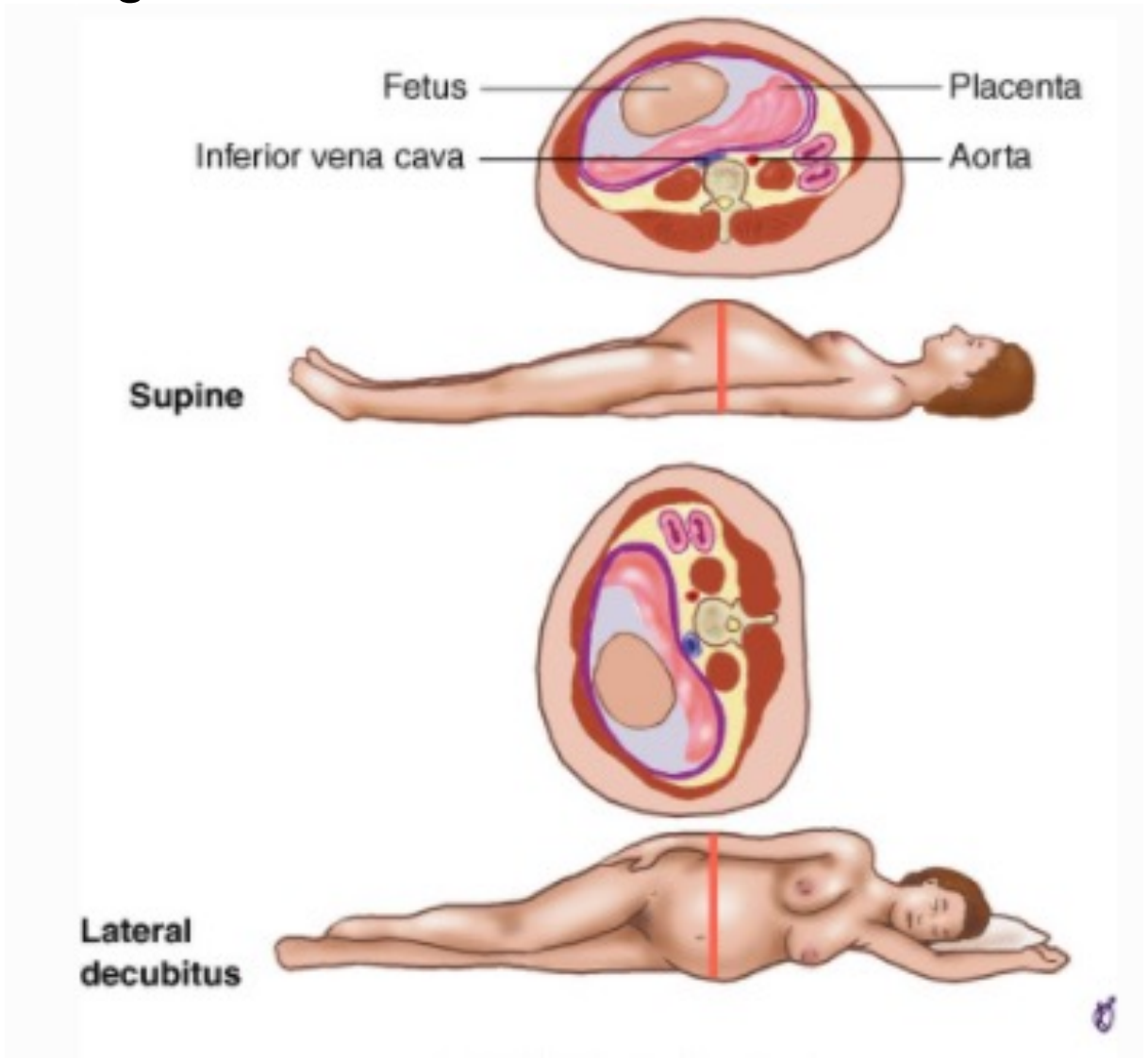




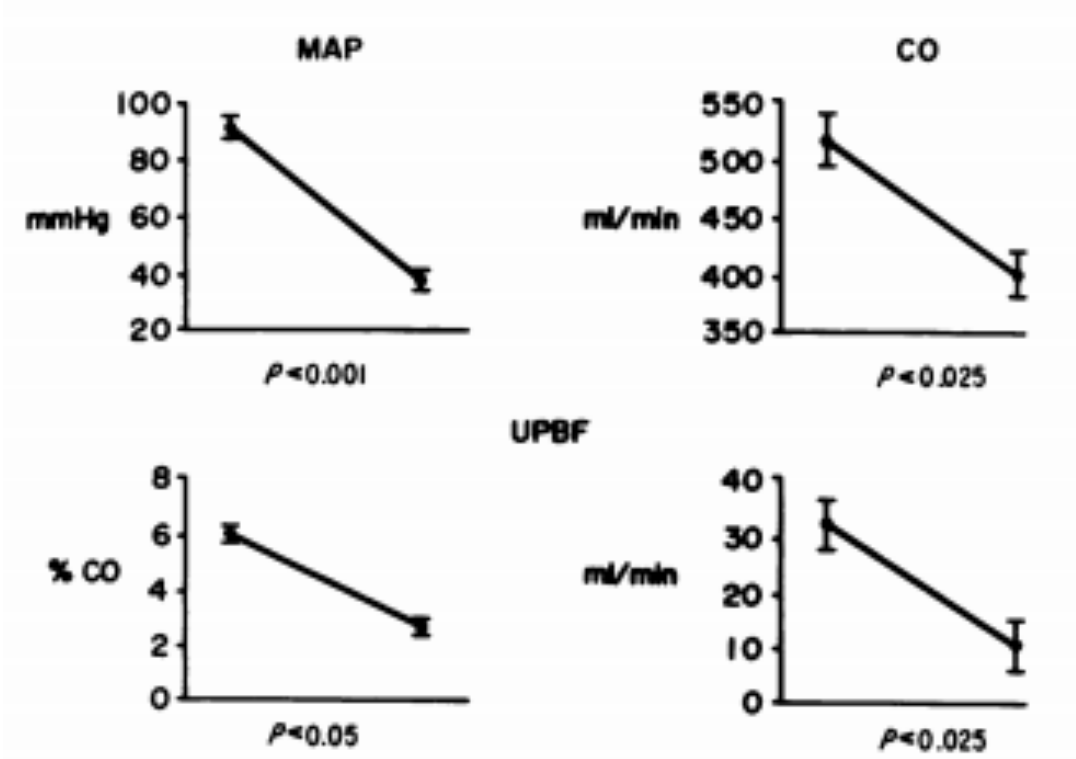
Intubation

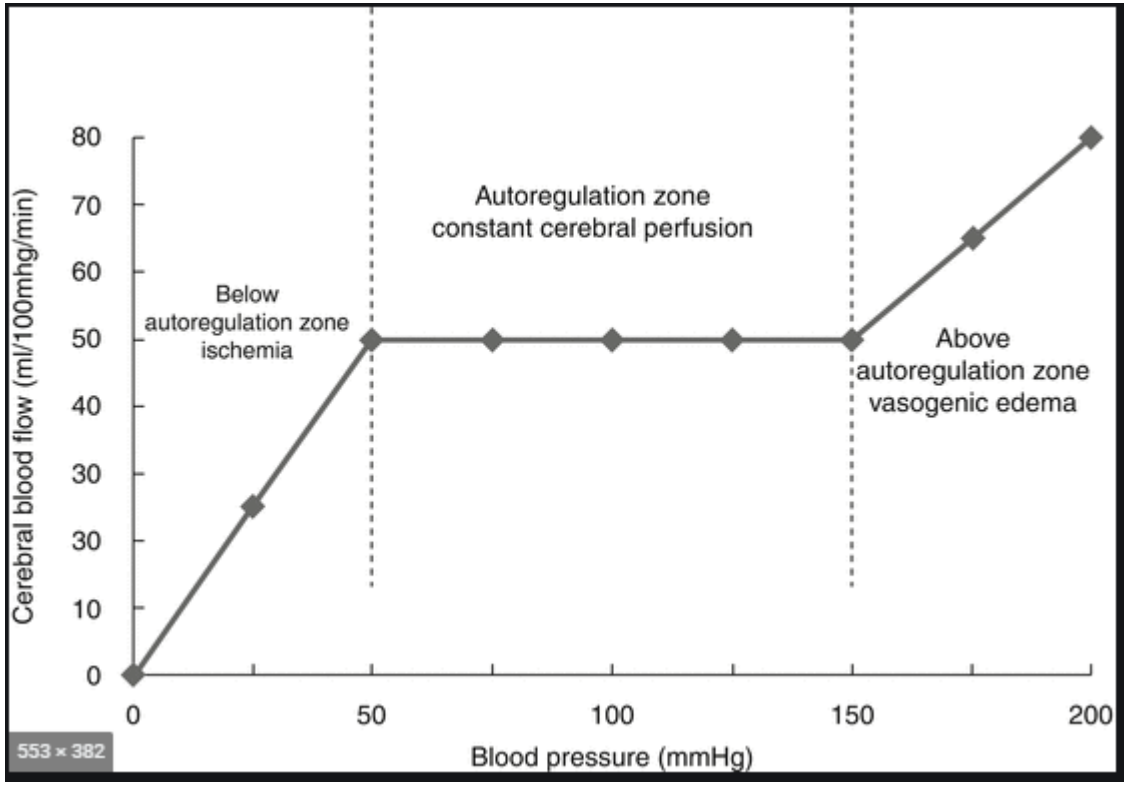
- Bipap is a safe ventilatory option
- Demand is high and reserve is low
- Rapid hypoxia-Preoxygenate
- Difficult airway-anterior and narrow, edema, aspiration
- Avoid nasal intubation-nasopharengyl congestion
- No autoregulation of uterine blood flow-maintain perfusing BP
- Have OB/peds at the bedside

Patient positioning



Autoregulation of placental perfusion



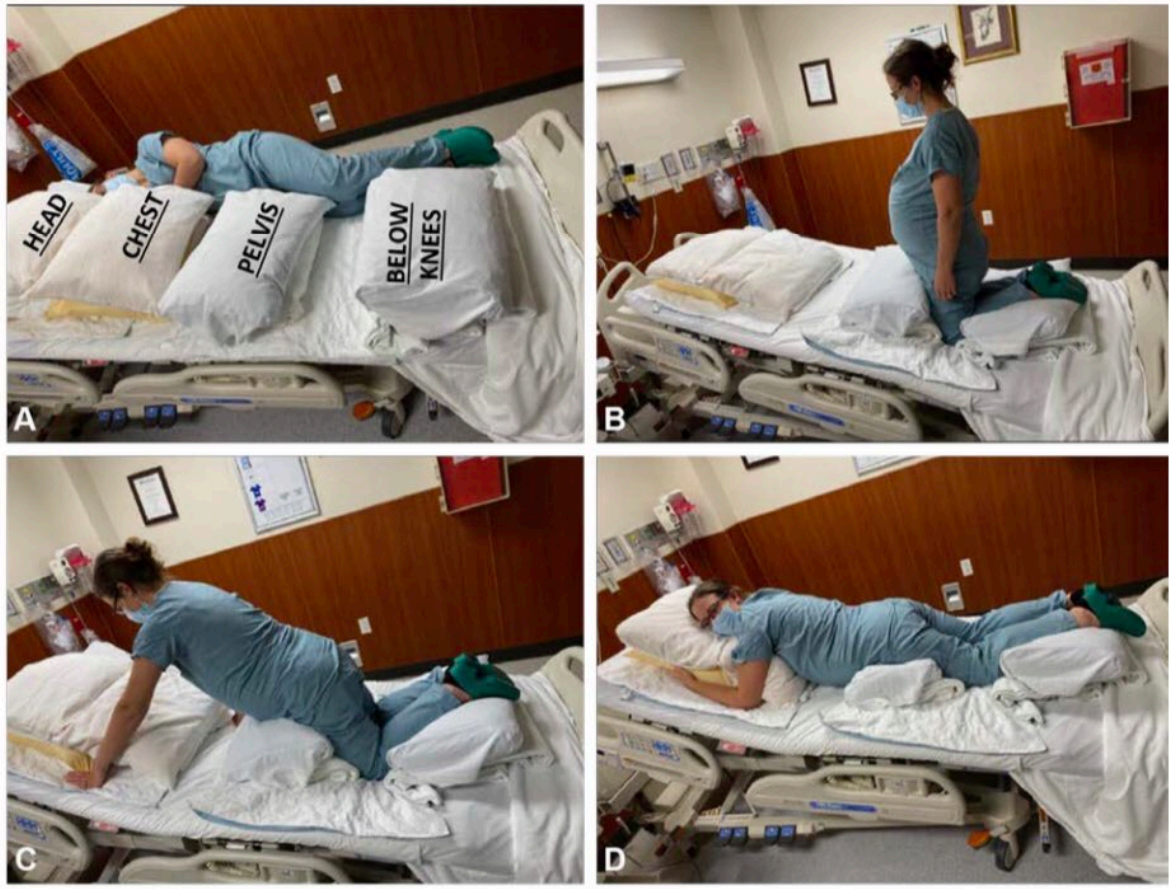


Ventilation in Pregnancy

What is different?

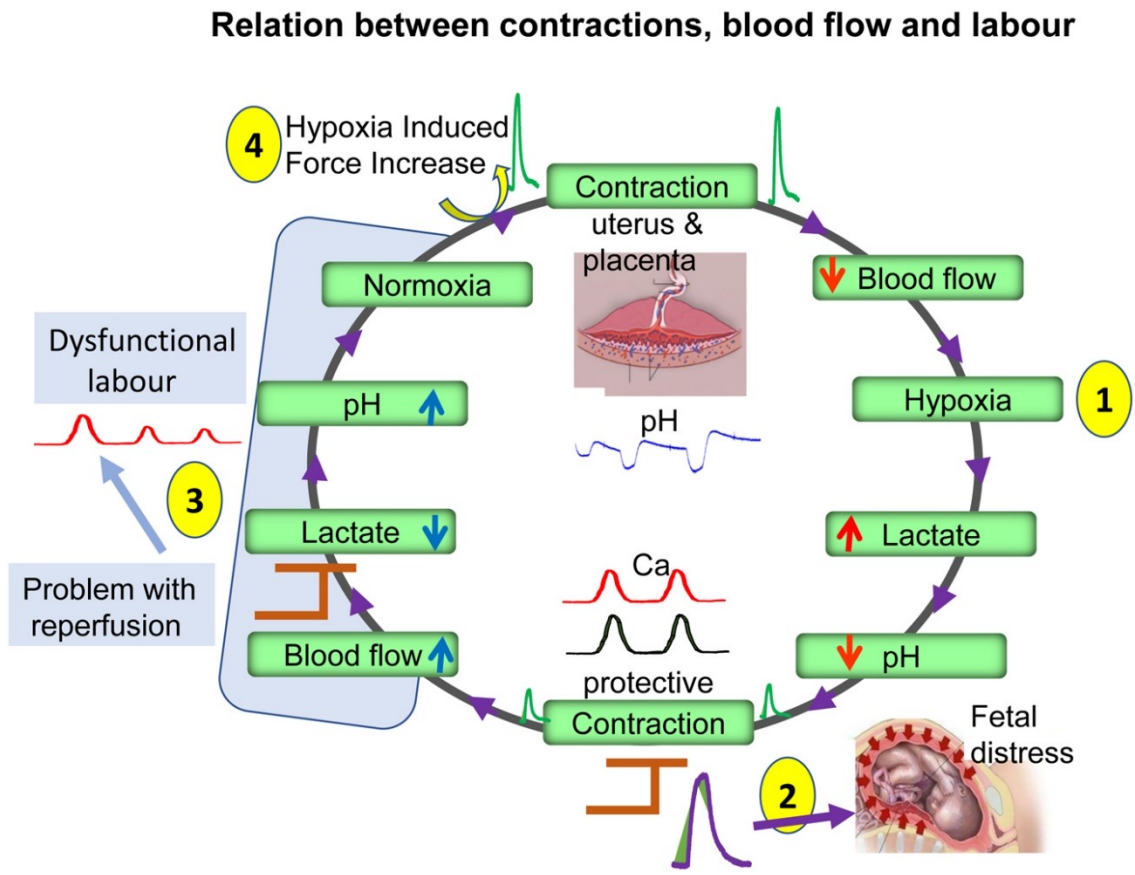
- Minute ventilation and CO2 goals
- SpO2 goals
- Offload the IVC
- Prone positioning is safe in pregnancy
  - Adequate bolstering is required to avoid abdominal compression
- Pulmonary vasodilator therapy can be used in pregnancy
  - Nitric oxide, sildenafil, and epoprostenol (IV and inhaled) are safe in pregnancy
  - Bonsentan is contraindicated
- Neuromuscular blockade is safe in pregnancy

Appendix 2. Prone positioning in awake pregnant patient. A. Patient lies on side facing towards the oxygen source. Adjust bed to reverse Trendelenburg (~10°). Place three pillows at head, two above gravid uterus, two at level of the pelvis (line up with symphysis pubis), and two under knees. B. Help patient kneel between two lower sets of pillows (lower leg pillows may be placed once she is prone). Ensure pelvic pillows are touching her thighs. Raise head of the bed. C. Help patient lie forward onto the pillows. D. Lower head of the bed (maintain reverse Trendelenburg). Adjust padding for patient comfort. Check gravid abdomen and ensure no pressure. Replace maternal and fetal monitors.



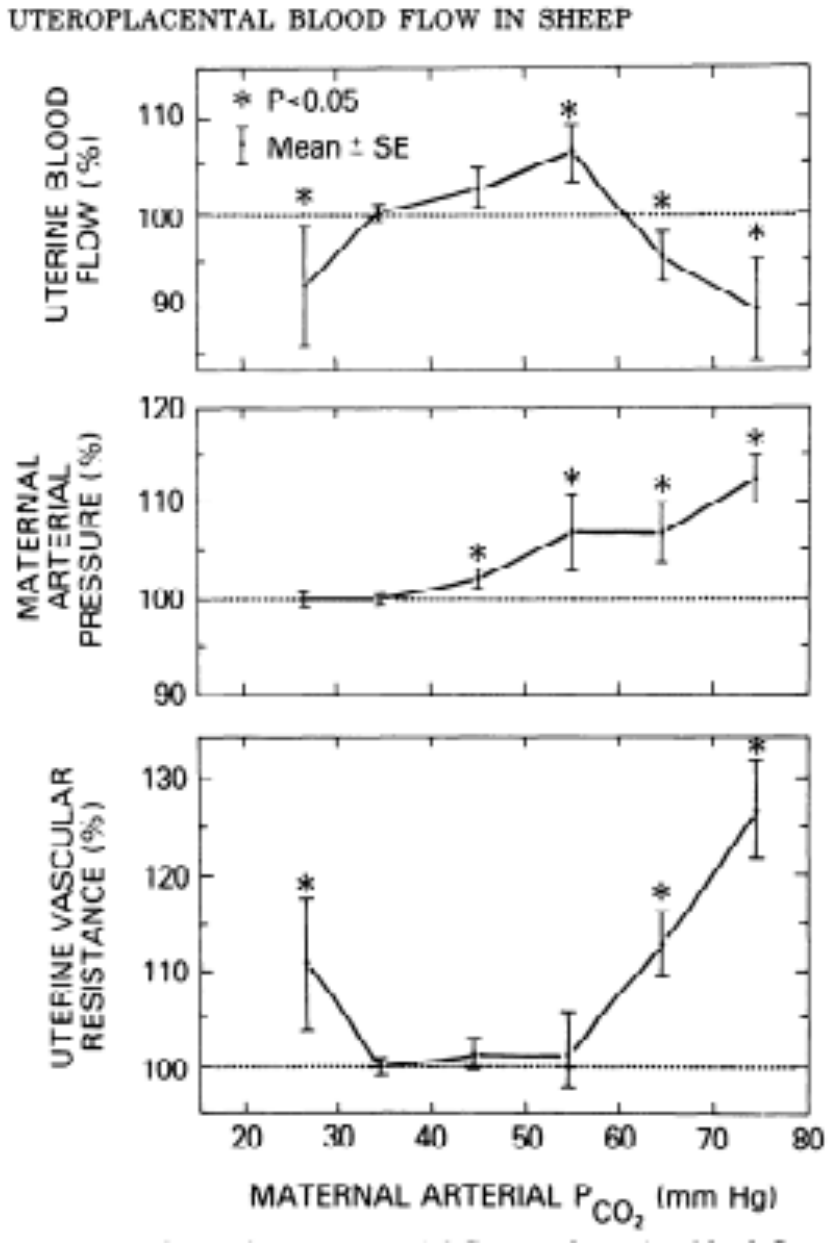
Hypoxia in pregnancy

- Short term effects:
  - HIE
  - Uterine contractions
  - Acidosis
- Long term
  - Fetal growth restriction
  - Oxidative damage
  - Placenta stress response pathways



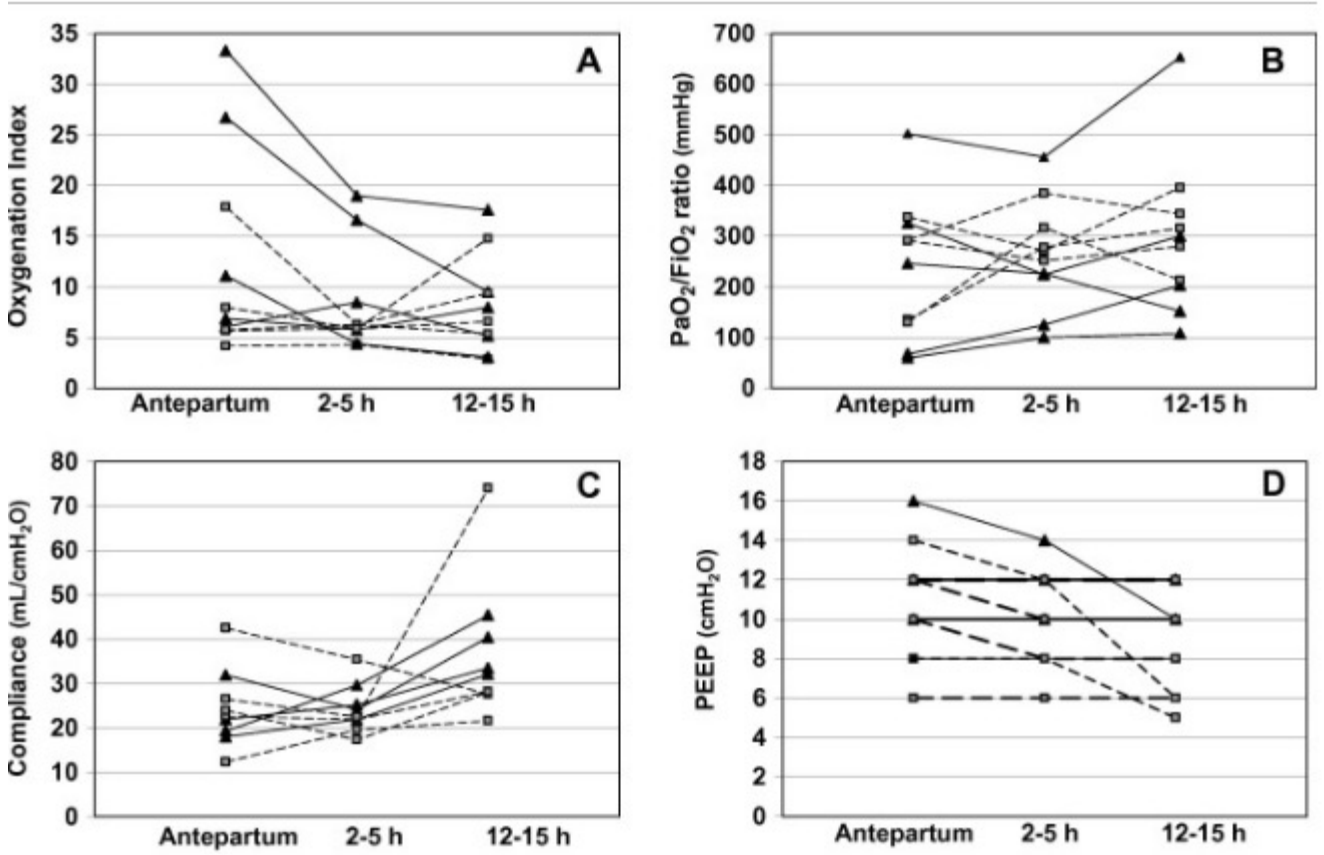
Permissive hypercapnia

- Fetal acidemia and hypoxic ischemic encephalopathy are closely associated
  Shifts O2 dissociation curve
- The fetus has a very limited buffer system
- Co2 must be offloaded across a concentration gradient
- Hypercarbia increases uterine artery resistance and decreases uterine artery blood flow



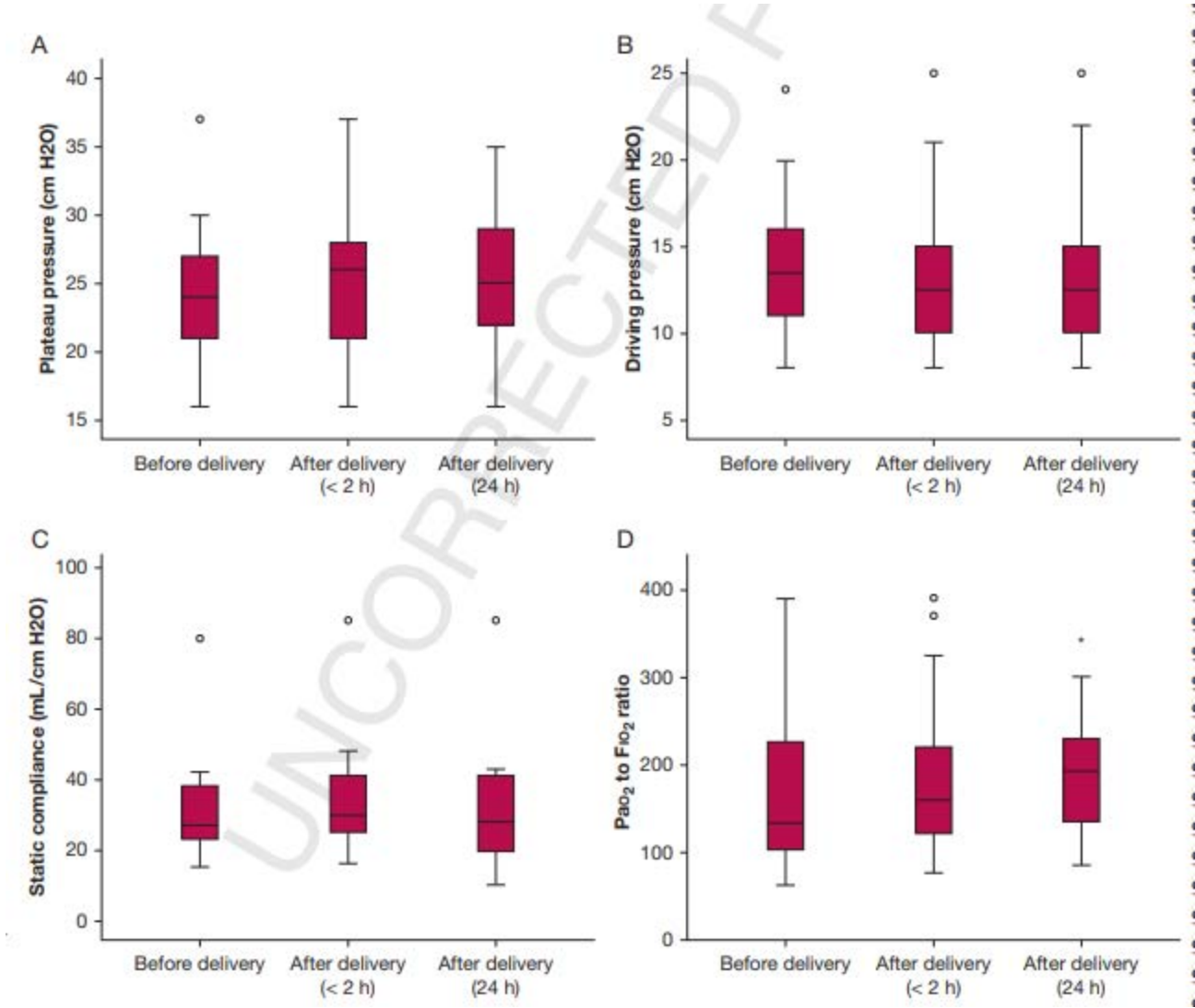
Does delivery improve Ventilation/oxygenation?

- Case series 10 patients requiring mech vent
- Pre COVID
- Mean GA 25 weeks

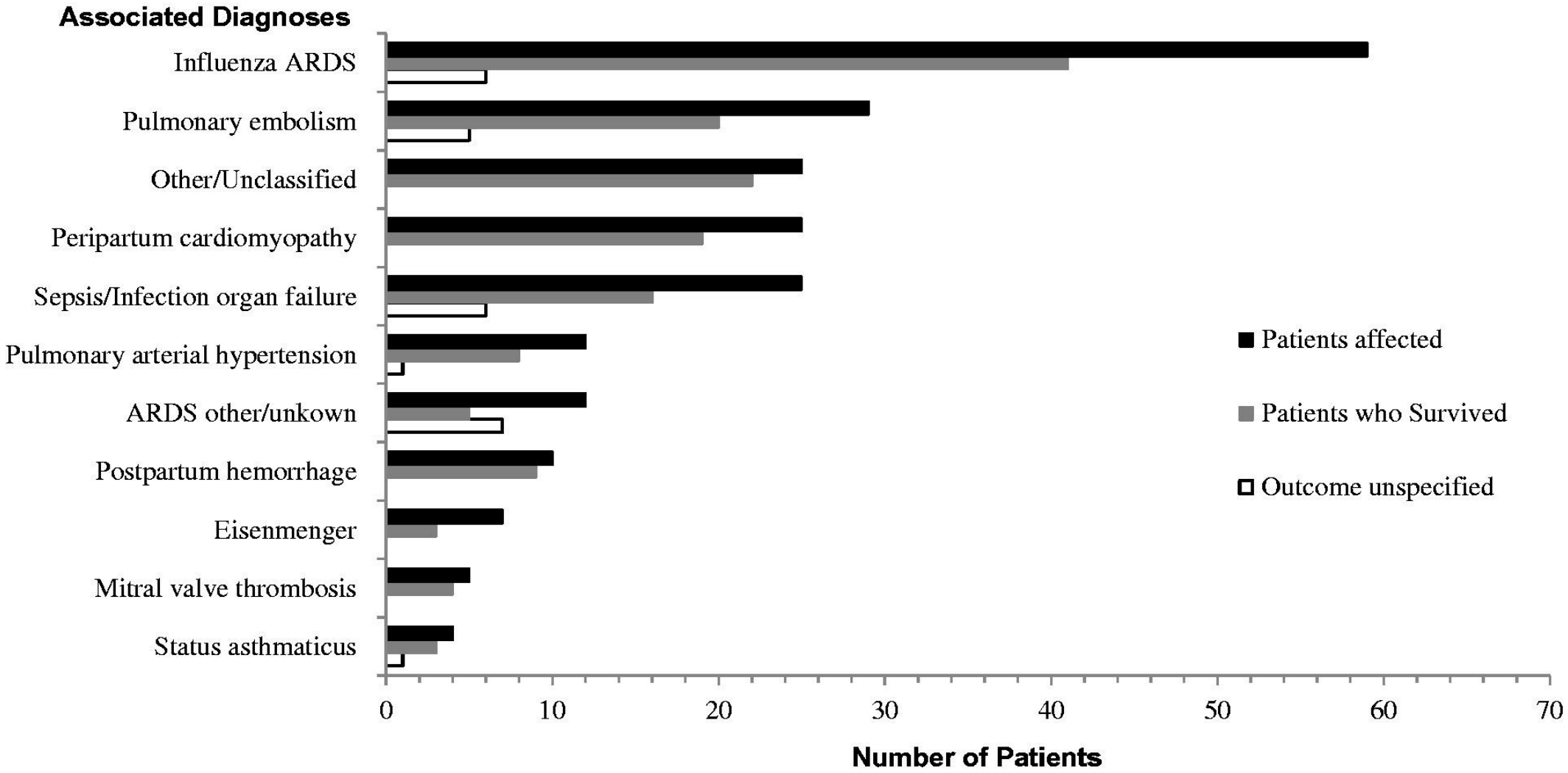


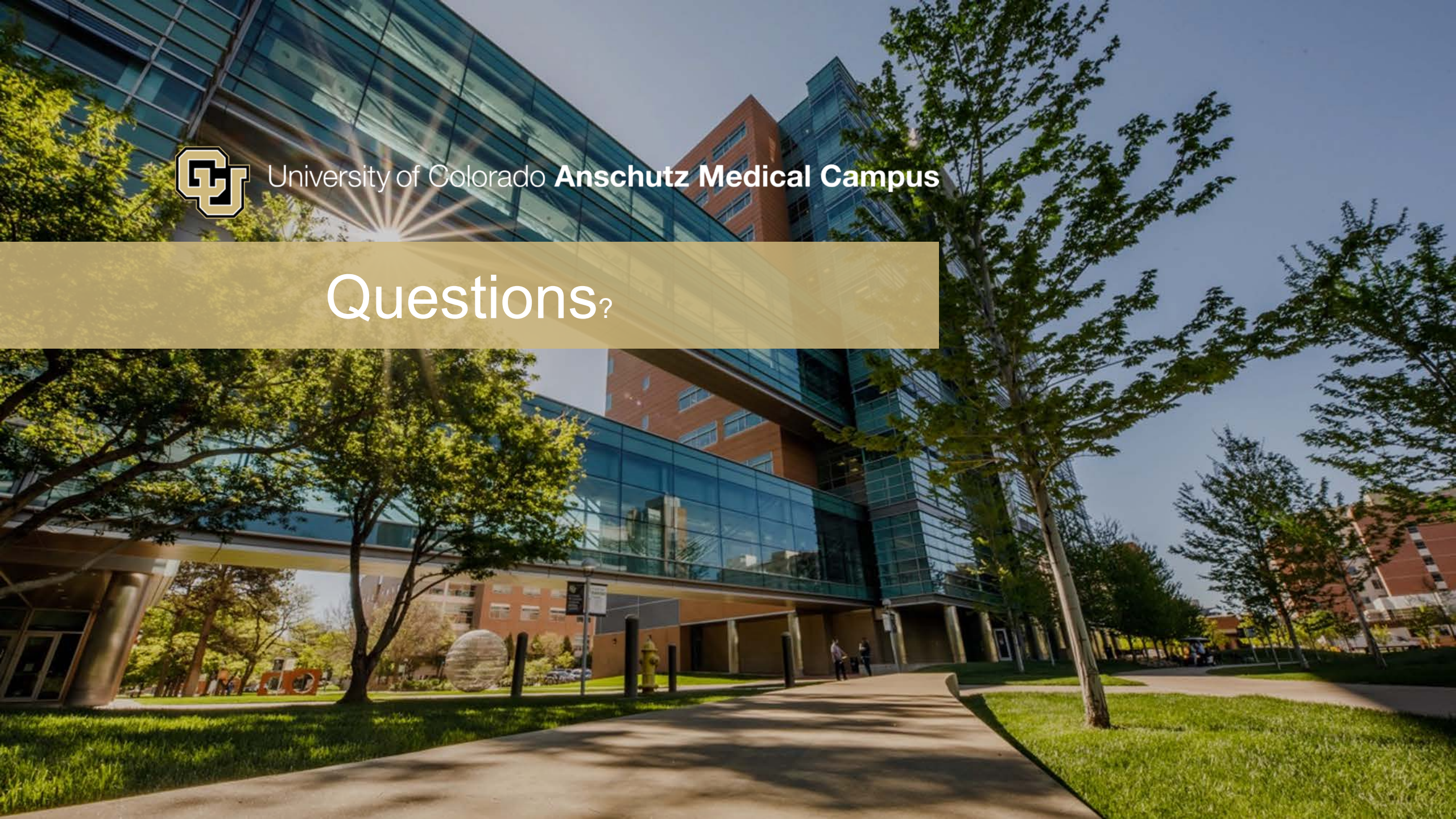
Does delivery improve ARDS?

- Data from COVID ARDS
- P:F improves 2 and 24 hrs after delivery
- Trend towards increased compliance
- No changes in driving pressure, PEEP, or plateau pressure



ECMO in Pregnancy





Questions?