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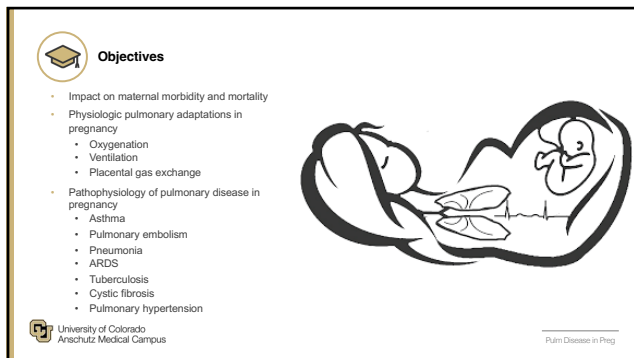
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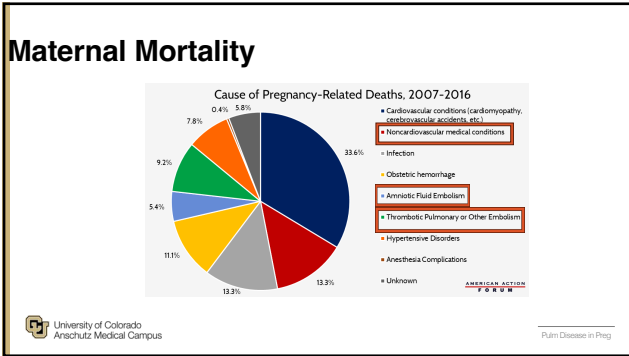
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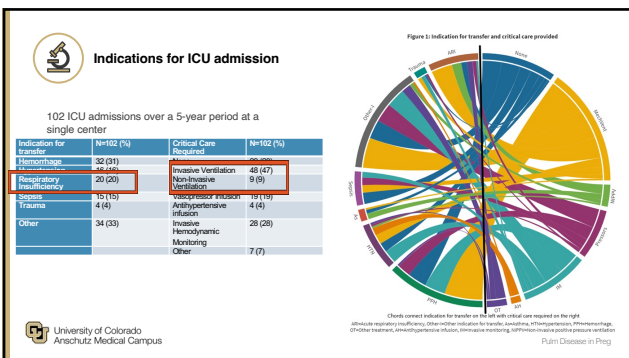
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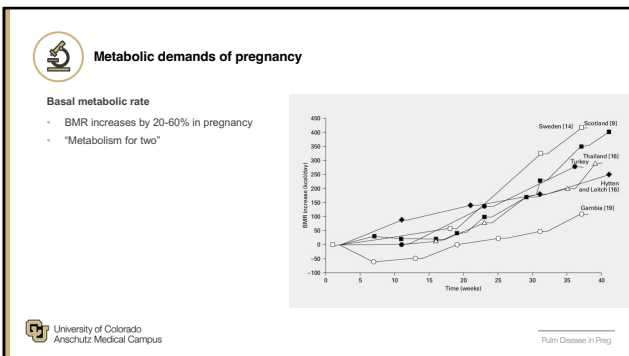
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### Metabolic demands of pregnancy

**BASAL METABOLIC RATE IN PREGNANCY**

Weeks Gestation	Oxygen Consumption (ml/min/24h)
20	220
24	230
28	240
32	250
36	255
38	260

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### 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

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### Carbon dioxide offloading

**Gradient dependent**

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

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### 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

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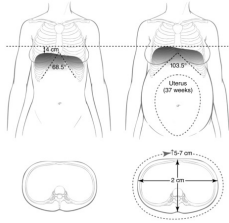
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### Physiologic changes in pregnancy



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

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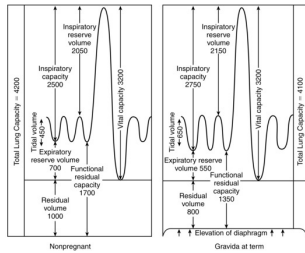
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Parameter	Change
<b>Thorax</b>	
Chest wall compliance	Decreased
Diaphragm compliance	Increased
Diaphragm	Elevated
Costochondrials	Unchanged
<b>Lung Volumes</b>	
Total lung capacity	Slightly increased
vital capacity	Slightly increased
inspiratory capacity	Slightly increased
functional residual capacity	Decreased
residual volume	Slightly decreased
expiratory reserve volume	Decreased
<b>Respiration</b>	
PaO <sub>2</sub> (arterial)	Unchanged
ventilation	Increased
minute ventilation	Increased
tidal volume	Increased
respiratory rate	Unchanged
<b>Other</b>	
pH	Normal
PaCO <sub>2</sub>	Slightly increased (due to)
PaO <sub>2</sub>	Slightly decreased (due to)
bicarbonate	Slightly decreased (due to)

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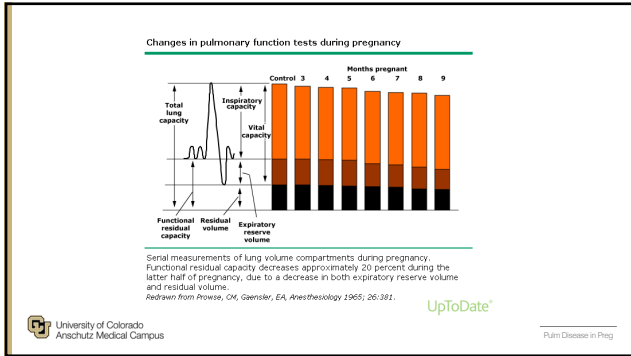
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### Asthma

**Reactive airway disease**

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

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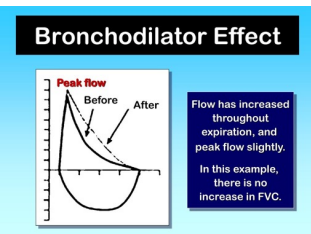
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**Asthma**


**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



**Bronchodilator Effect**

Flow has increased throughout expiration, and peak flow slightly. In this example, there is no increase in FVC.



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Components of Severity		Classification of Asthma Severity (Youths ≥12 years of age and adults)			
		Intermittent	Mild	Moderate	Severe
<b>Impairment</b>  Normal FEV <sub>1</sub> /FVC: 8-19 yr 85% 20-39 yr 85% 40-59 yr 75% 60-89 yr 75%	Symptoms	≤2 day/week	≤2 day/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2/month	3-4/month	>1/week but not nightly	Often 7x/week
	Short-acting beta <sub>2</sub> -agonist use for symptom control (not prevention of EOs)	≤2 day/week	>2 day/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 <sub>1</sub> between exacerbations • FEV <sub>1</sub> ≥80% predicted • FEV <sub>1</sub> /FVC normal	• FEV <sub>1</sub> ≥80% predicted • FEV <sub>1</sub> /FVC normal	• FEV <sub>1</sub> >60% but <80% predicted • FEV <sub>1</sub> /FVC reduced 5%	• FEV <sub>1</sub> <60% predicted • FEV <sub>1</sub> /FVC reduced >5%	
<b>Risk</b>	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 <sub>1</sub> .		



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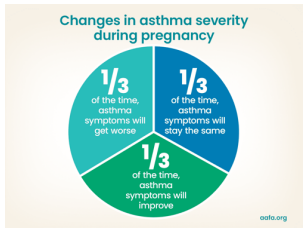
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**Asthma**

**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




**Changes in asthma severity during pregnancy**

1/3 of the time, asthma symptoms will get worse

1/3 of the time, asthma symptoms will stay the same

1/3 of the time, asthma symptoms will improve

asthma.org



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**Asthma**

**Effects of asthma on Pregnancy**

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Substance	No asthma n = 296,448 # (%)	Asthma n = 17,744 # (%)	P value*	Site-adjusted relative risk (95% CI)†	Fully adjusted relative risk (95% CI)‡
<b>Maternal outcomes</b>					
Prevalence duration of pregnancy					
Spontaneous preterm birth	688 (0.8)	219 (1.3)	< .0001	1.64 (1.33-1.99)	1.34 (1.15-1.56)
Colostrum	207 (0.1)	20 (0.2)	.01	1.61 (1.16-2.24)	1.41 (1.08-1.93)
Pneumonia	9028 (4.7)	924 (5.4)	< .0001	1.24 (1.16-1.33)	1.14 (1.06-1.23)
Cardiometabolic hypertension	9323 (2.7)	507 (3.3)	.0003	1.19 (1.09-1.30)	1.08 (1.00-1.18)
<b>Maternal adverse</b>					
All maternal outcomes	176 (0.1)	33 (0.2)	.0008	1.91 (1.33-2.63)	1.79 (1.21-2.63)
Maternal adverse without hypertension-related	61 (0.03)	14 (0.08)	.19	1.48 (0.93-2.33)	1.38 (0.97-1.93)
Maternal adverse with hypertension-related	65 (0.03)	19 (0.12)	.0006	2.01 (1.49-2.70)	2.07 (1.47-2.93)
<b>Other pregnancy complications</b>					
Gestational diabetes	10,420 (3.1)	807 (4.6)	.08	1.07 (1.00-1.15)	1.11 (1.03-1.19)
Chromosomes	4415 (1.1)	504 (2.8)	.32	1.05 (0.95-1.16)	1.08 (0.96-1.21)
Placenta previa	1444 (0.7)	141 (0.8)	.08	1.19 (0.99-1.42)	1.20 (1.00-1.39)
<b>Complications of labor and delivery</b>					
Prelabor cesarean delivery	29,688 (11.9)	2160 (12.9)	< .0001	1.15 (1.10-1.21)	1.10 (1.04-1.17)
Cesarean labor	111,522 (34.6)	8021 (45.2)	< .0001	1.08 (0.94-1.24)	1.07 (0.94-1.24)
Cesarean delivery after spontaneous labor	18,835 (6.1)	1740 (10.3)	.0003	1.10 (1.05-1.16)	1.08 (1.00-1.17)
Vaginal	71,220 (24.6)	5988 (34.9)	< .0001	1.10 (1.06-1.15)	1.10 (1.04-1.16)
Cesarean delivery after induction	14,746 (5.1)	1393 (8.1)	< .0001	1.22 (1.14-1.30)	1.17 (1.09-1.26)
All vaginal delivery	140,189 (72.8)	11,729 (68.8)	< .0001	0.84 (0.81-0.87)	0.84 (0.80-0.87)
<b>Fetal/Neonatal</b>					
Preterm	4098 (2.2)	1463 (8.3)	< .0001	1.23 (1.17-1.29)	1.10 (1.01-1.20)
PCPN	14,379 (2.6)	1212 (7.3)	.08	1.08 (0.94-1.24)	0.99 (0.83-1.09)
Birth presentation	9708 (4.3)	811 (4.6)	.01	1.10 (1.03-1.18)	1.12 (1.05-1.20)
Placental abruption	2342 (0.8)	360 (2.1)	< .0001	1.27 (1.14-1.42)	1.22 (1.09-1.36)
Maternal hemorrhage	13,429 (4.5)	1260 (7.1)	.001	1.11 (1.04-1.18)	1.08 (1.01-1.16)
Maternal pulmonary embolism	114 (0.04)	20 (0.12)	.04	1.80 (1.19-2.73)	1.71 (1.05-2.79)
Maternal postpartum fever	6531 (2.7)	532 (3.3)	.38	1.05 (0.95-1.16)	0.99 (0.90-1.09)
Maternal ICU admission	902 (0.6)	73 (0.4)	.01	1.30 (1.04-1.70)	1.24 (1.04-1.47)
Maternal death	18 (0.01)	1 (0.01)	.79	Not available	Not available
Low birthweight, <2500 g	16,331 (5.1)	1015 (5.7)	< .0001	1.20 (1.18-1.23)	1.10 (1.07-1.13)
Neonatal death, <27 wk	20,618 (6.8)	2038 (11.6)	< .0001	1.20 (1.18-1.23)	1.17 (1.13-1.23)
Perinatal death, <28 wk	21,618 (6.8)	2124 (12.0)	.01	1.13 (1.05-1.22)	1.07 (0.97-1.17)

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**Asthma**

**Treatment**

- Avoiding triggers
- Continuing pregnancy 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%

Blow out hard and fast in a single blow

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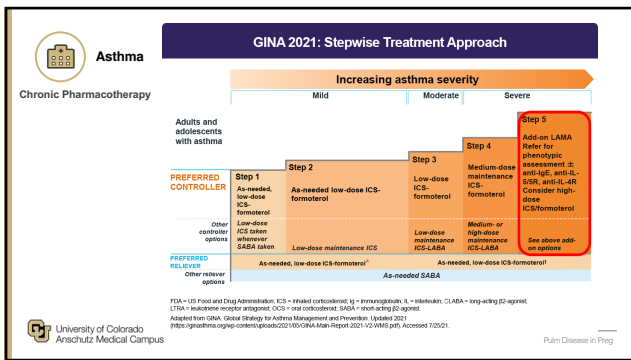
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Medication	Low dose	Medium dose	High dose
<b>ICS/LABA combination</b>			
<b>Budesonide/albuterol HFA (Brand name: Airspira)<sup>†</sup></b>			
NOTE: Not used for maintenance therapy.			
Adult (pregnant and non-pregnant): Budesonide/albuterol (80 mcg/90 mcg) 2 inhalations as needed (usual maximum: 12 inhalations/day).			
<b>ICS/LABA combination</b>			
<b>Becloethasone (Beclomethasone)/formoterol DPI or HFA (Not available in United States or Canada, but available elsewhere (sample brand names: Formoterol, Forastal, Foster))<sup>†</sup></b>			
100 mcg/20 mcg	1 inhalation twice a day	2 inhalations twice a day	
200 mcg/20 mcg			2 inhalations twice a day
<b>Budesonide/formoterol HFA (Brand names: Symbicort, Brinjaya)<sup>†</sup></b>			
80 mcg/2 mcg	2 inhalations twice a day		
160 mcg/4 mcg		2 inhalations twice a day	
<b>Fluticasone furoate (Fluticasone)/glicoxal DPI (Not available in United States or Canada, but available elsewhere (sample brand name: Adair))<sup>†</sup></b>			
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
<b>Fluticasone propionate/formoterol MDI (Not available in United States or Canada, but available elsewhere (sample brand name: Flutiform))</b>			
50 mcg/5 mcg	2 inhalations twice daily		
125 mcg/5 mcg		2 inhalations twice daily	
250 mcg/5 mcg			2 inhalations twice daily
<b>Fluticasone propionate/salmeterol DPI (Brand names: Advair Diskus, Wixela Inhaled)<sup>†</sup></b>			
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
<b>Fluticasone propionate/salmeterol HFA (Brand name: Advair HFA)<sup>†</sup></b>			
45 mcg/21 mcg	2 inhalations twice a day		
113 mcg/21 mcg		2 inhalations twice a day	
230 mcg/21 mcg			2 inhalations twice a day

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### Asthma

**Less common meds in pregnancy**

- Theophylline
  - Phosphodiesterase and adenosine receptor blocker
  - Lots of side effects
  - Requires blood level monitoring
- Leukotriene modulators (montelukast)
  - 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



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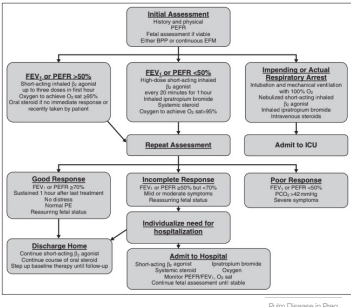
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### Asthma

**Treating an acute exacerbation**

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



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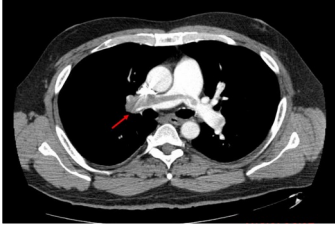
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## Pulmonary embolism



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### Pulmonary embolism

**Epidemiology**

- 6<sup>th</sup> 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

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### 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

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**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.

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**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 (J-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, MSc, Molly J. Stout, MD, Gregg A. Manning, MD, MSc, and Sanjeev Bhatia, MD

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**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 (3* to 5** weeks)	Time Post Conception (6* to 13** weeks)	Time Post Conception (14* to 23** weeks)	Time Post Conception (24* week to term)
< 0.10 Gy (10 rad)	Non-cancer health effects NOT detectable.				
0.10–0.50 Gy (10–50 rad)	Fetus to infant may increase slightly, but surviving embryos will probably have an 80% health span-cancer health effects.	Growth restriction possible.	Growth restriction possible.	Non-cancer health effects unlikely.	
> 0.50 Gy (50 rad)	Failure to implant will likely be high depending on dose, but surviving embryos will probably have no significant cancer health effects.	Probability of miscarriage may increase, depending on dose.	Probability of miscarriage may increase, depending on dose. Growth restriction is likely.	Probability of miscarriage may increase, depending on dose. Less likely than during the first trimester. Growth restriction is possible if probability of major malformations may increase.	Miscarriage and neonatal death may occur, depending on dose.

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### 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% (50)
Submassive	Systolic pressure > 90 mm Hg and either (a) RV dysfunction (CT, BNP, troBNP, ECG changes) or (b) myocardial necrosis (elevated troponin)	3% (20)
Low risk	Absence of hypotension, RV dysfunction, and myocardial necrosis	<1% (20)

Note:—BNP = brain natriuretic peptide; CT = electrocardiography

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### 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

**A-OK Protocol: Proposed Mechanism**

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## Pulmonary Hypertension



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## Pulmonary Hypertension

- Heterogenous group of diseases (Hemmes, 2015)
  - Characterized by mPAP  $\geq 25$  mmHg
  - May be accompanied by increase of pulmonary vascular resistance
  - WHO classification

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## 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, scleroderma-associated PAH, precocious PH of the newborn
Group 2	PH due to left heart disease	Left ventricular systolic dysfunction, left ventricular diastolic dysfunction, acute or chronic 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.<sup>1</sup>

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# Pulmonary Hypertension

- Improved outcomes in modern era, but mortality remains high <sup>(Hermes, 2015)</sup>
  - 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

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# Pulmonary Hypertension

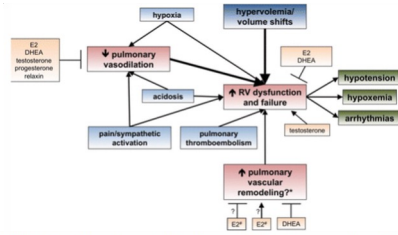


Figure 3. Pathophysiology of pulmonary hypertension (PH) and right ventricular (RV) dysfunction in pregnancy. Items in red represent the underlying presenting alterations in PH. Items in blue represent pregnancy-related alterations that may aggravate these alterations. Potential contributions of sex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

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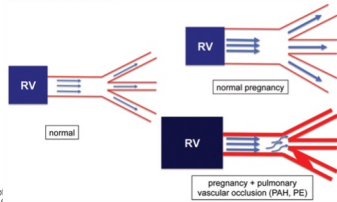
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# Pulmonary Hypertension

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 flow 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 (Hemmes, 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

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### Pulmonary Hypertension

- Well, she's pregnant.

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### Pulmonary Hypertension

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

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## Pulmonary Hypertension

- Genetic counseling (Hennes, 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

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## Pulmonary Hypertension

- Pregnancy management (Hennes, 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
  - Epidural or spinal recommended over general
  - Avoid vasalvagal triggers

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## Pulmonary Hypertension

- Medications (Hennes, 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

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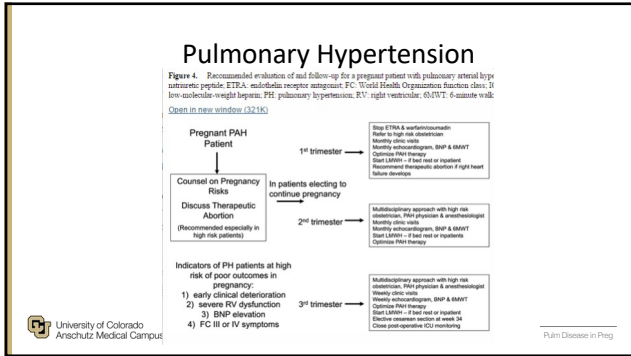
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### Pulmonary Hypertension

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

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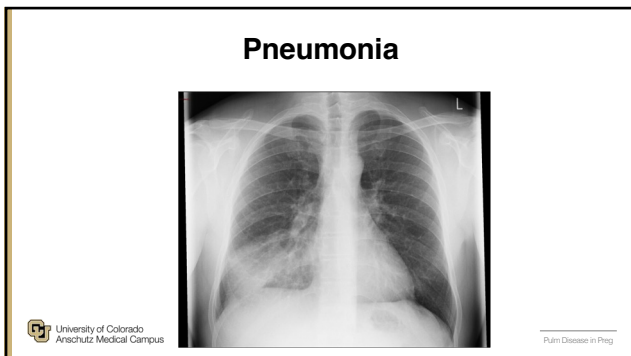
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**Pneumonia**

- 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

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**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: pyelonephritis, appendicitis, PTL
- Diagnosis by CXR

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**Pneumonia**

- Pathogens (Lim 2010)
  - Bacterial
    - S. pneumoniae 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

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## 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, hydrocephaly, cardiac anomalies
      - Attenuated with use of anti-pyretic
  - Also associated with poor obstetrical outcome
    - SAB, PTD, IUGR, IUFD

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## 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

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## Pneumonia

- Pathogens (Lim 2010)
  - Fungal
    - Rare in pregnancy
    - Coccidioidomycosis
      - 10 cases over 6 years
      - Greater risk for dissemination
      - High mortality if acquired in 3T
    - Cryptococcus
      - 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

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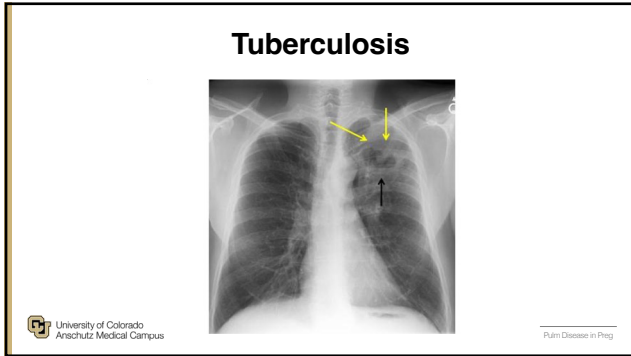
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**Tuberculosis**

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

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**Tuberculosis**

- **Diagnosis** (Labi 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

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## Tuberculosis

- **Testing** (Worighoh 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


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## 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


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## Tuberculosis

- **Congenital TB is very rare** (Marji 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%


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### 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

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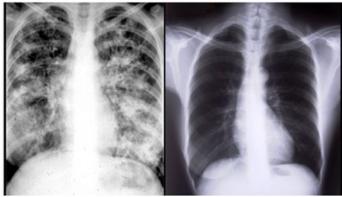
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### Cystic Fibrosis



Cystic Fibrosis Lung

Healthy Lung

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### Cystic Fibrosis

- Background <sup>(Pate, 2015)</sup>
  - Autosomal recessive disorder affecting 1 in 3,500 births
  - 2000 genes identified
  - 1/25 carrier rate in Caucasians
  - 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

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### 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

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### 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

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### 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)

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### 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

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### ARDS




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### 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

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**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<sub>2</sub>/FIO<sub>2</sub> >200 mmHg, but ≤300 mmHg, PEEP/CPAP ≥5 cm H<sub>2</sub>O
    - Moderate ARDS:
      - » PaO<sub>2</sub>/FIO<sub>2</sub> >100 mmHg, but ≤200 mmHg, PEEP ≥5 cm H<sub>2</sub>O.
    - Severe ARDS:
      - » PaO<sub>2</sub>/FIO<sub>2</sub> ≤100 , PEEP ≥5 cm H<sub>2</sub>O

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**ARDS**

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

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**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

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## 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"

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## 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

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### 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
<ul style="list-style-type: none"> <li>• Need to secure airway</li> <li>• Depressed sensorium</li> <li>• Imperfect airway reflexes</li> <li>• Upper airway instability after trauma</li> <li>• Decreased airway patency</li> <li>• Need for sedation in a situation of poor airway control</li> <li>• Imaging (CT, MRT) and transportation of the patient</li> </ul>	<ul style="list-style-type: none"> <li>• Hypoxia: acute hypoxemic respiratory failure</li> <li>• Hypoventilation</li> <li>• Unacceptably high work of breathing</li> <li>• Hemodynamic compromise</li> <li>• Cardiorespiratory arrest</li> <li>• Refractory shock</li> <li>• Raised intracranial pressure</li> <li>• Flail chest</li> </ul>

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### Intubation in Pregnancy

- 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-nasopharyngeal congestion
- No autoregulation of uterine blood flow-maintain perfusing BP
- Have OB/peds at the bedside



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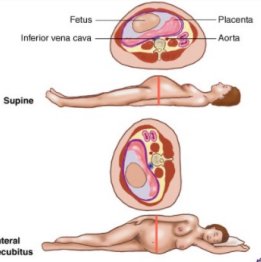
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### Patient positioning



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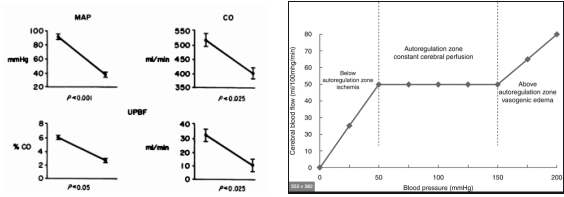
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### Autoregulation of placental perfusion



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### Ventilation in Pregnancy

**What is different?**

- Minute ventilation and CO2 goals
- SpO2 goals
- Offload the IVC
- Prone positioning is safe in pregnancy  
Adequate bolsting 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  
Bosentan 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 (15°). Place three pillows at head, two above gravid uterus, two at level of the pelvis (one up with symphysis pubis), and two under knees. B. Help patient lie 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 (maintains reverse Trendelenburg). Adjust padding for patient comfort. Check gravid abdomen and ensure no pressure. Replace maternal and fetal monitors.

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### Hypoxia in pregnancy

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

**Relation between contractions, blood flow and labour**

4 Hypoxia Induced Force Increase → Contraction ↑ → Blood flow ↓ → Hypoxia ↑ → Fetal distress ↑

Normoxia → Contraction ↓ → Blood flow ↑ → Hypoxia ↓ → Fetal distress ↓

5 Problem with reperfusion → Blood flow ↓ → Lactate ↑ → pH ↓ → Fetal distress ↑

3 Dysfunctional labour → Contraction ↑ → Blood flow ↓ → Hypoxia ↑ → Fetal distress ↑

2 Contraction ↑ → Blood flow ↓ → Hypoxia ↑ → Fetal distress ↑

1 Hypoxia ↑ → Contraction ↑ → Blood flow ↓ → Hypoxia ↑ → Fetal distress ↑

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### 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

**UTEROPLACENTAL BLOOD FLOW IN SHEEP**

UTERINE BLOOD FLOW (%) vs MATERNAL ARTERIAL P<sub>a</sub>CO<sub>2</sub> (mm Hg)

MATERNAL PRESSURE (%) vs MATERNAL ARTERIAL P<sub>a</sub>CO<sub>2</sub> (mm Hg)

UTERINE VASCULAR RESISTANCE (%) vs MATERNAL ARTERIAL P<sub>a</sub>CO<sub>2</sub> (mm Hg)

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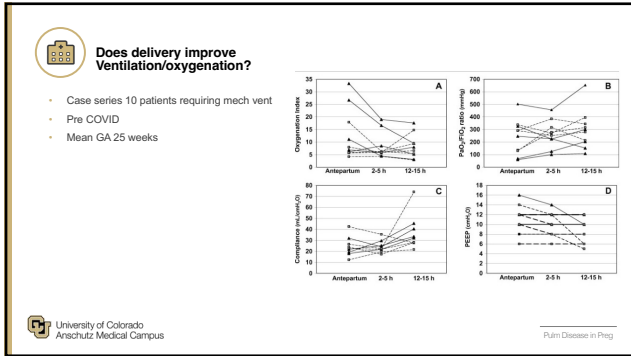
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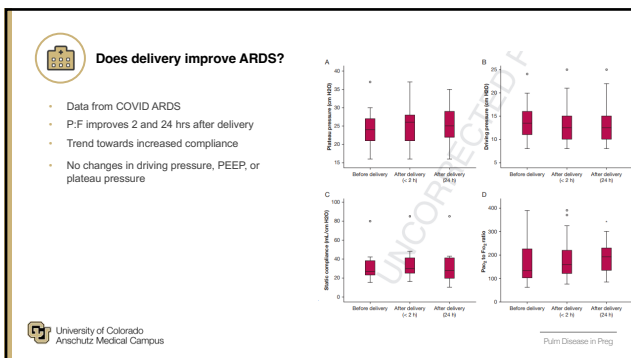
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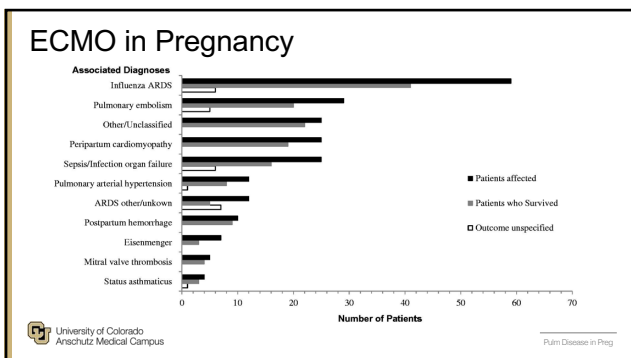
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