ASTHMA IN PREGNANCY

FLAME LECTURE: 89

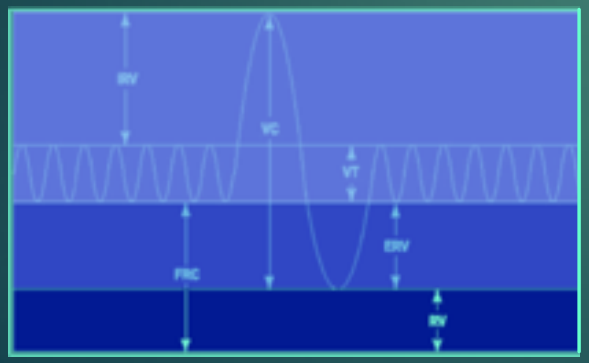
BURNS 5.14.19

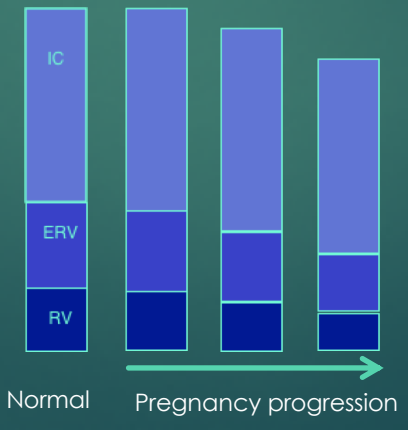
OBJECTIVES

- Identify asthma in pregnancy and discuss potential impact on the gravid patient and the fetus/newborn
- Discuss the impact of pregnancy on each condition
- Discuss the appropriate initial evaluation
- Prerequisites:
  - FLAME 25: Respiratory physiology during pregnancy
- See also:
  - NONE

REVIEW OF RESP PHYSIO IN PREG

- FVC, FEV_1, and peak expiratory flow all stay relatively the same during pregnancy
- RV, ERV (and thus **FRC**) are ↓ due to diaphragm elevation from enlarging uterus
- VC and TLC remain unchanged until late pregnancy
  - IC initially increases slightly to offset FRC decrease and maintain TLC
- TV increased, resulting in increased minute ventilation
- Progesterone also stimulates respiratory drive & ventilation





Are these acronyms confusing? See the FLAME 25 – Respiratory Physiology in Preg before proceeding!

REVIEW OF RESP PHYSIO IN PREG

- The increase in minute ventilation allows for more CO_2 to be blown off causing a mild respiratory alkalosis
- Benefits of respiratory alkalosis?
  - The fetus not only depends on the maternal respiratory system for obtaining O_2, but also for CO_2 excretion; thus, decreased maternal P_{CO2} creates a gradient that allows the fetus to offload CO_2
  - This is partially compensated with increased maternal renal loss of HCO_3, but blood gasses are still shifted during pregnancy

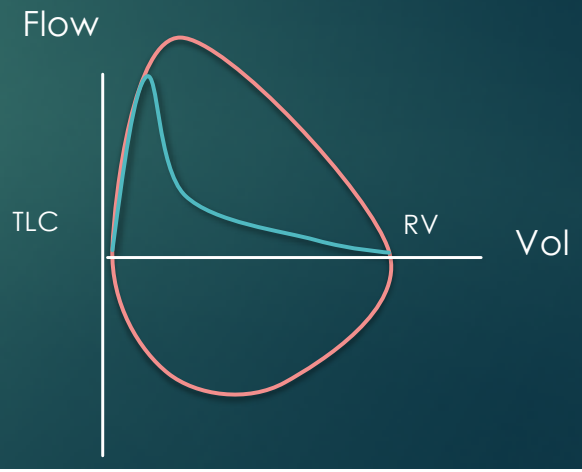
ABG	NON-PREGNANT	PREGNANT
pH	7.38-7.42	7.39-7.45
pCO_2	38-42	25-33
pO_2	90-100	92-107
BICARB	22-26	16-22

Thus, in a pregnant patient with asthma, altered blood gasses are much scarier to interpret because a pregnant patient with a P_{CO2} of 42 is already retaining and this can be mistaken for normal!!!!

GENERAL ASTHMA PHYSIOLOGY

- Hypersensitivity to a trigger results in bronchospasm and airway constriction
- Inflammation and reactive mucous production contribute to further airway narrowing
- This causes primarily obstructive pulmonary dysfunction → obstructive exhalation (i.e a ↓ in FEV_1) → a ↓ in **FEV_1/FVC**

- Lung volumes in asthmatics
  - RV most increased and takes longest to recover on therapy
  - FRC increased due to hyperinflation
  - TLC normal or elevated (loss of lung recoil)



CLASSIFICATION

Classification	Symptom Frequency	Night time Awakening	Interference with normal activity	FEV_1 or PEFR (Predicted % of personal best)
Mild Intermittent	0-2 days/week	0-2 times/month	None	> 80%
Mild Persistent	3-6 days/week	3-4 times/month	Minor limitation	> 80%
Moderate Persistent	Daily	2-3 times/week	Some limitation	60-80%
Severe Persistent	Throughout the day	>3 times/week	Extreme limitation	<60%

Severity and control of asthma should also be assessed in terms of symptom exacerbation and pulmonary impairment: prior hospitalization? ICU admissions? Intubations? ED visits? Past oral corticosteroid requirements?

EFFECT OF PREGNANCY ON ASTHMA

- Effect of pregnancy on asthma is variable. In general:
  - ~30% of patients asthma symptoms worsen
    - Most exacerbations occur from 20-36 weeks
  - ~25% of patients have symptoms improve
    - Symptoms most improved during last 4 weeks of pregnancy
  - ~45% of patients notice no change in symptoms

Classification	Exacerbation Rate During Pregnancy	Hospitalization Rate During Pregnancy
Mild Intermittent **Mild Persistent**	12.6%	2.3%
Moderate Persistent	25.7%	6.8%
Severe Persistent	51.9%	26.9%

Schatz 2003

EFFECT OF PREGNANCY ON ASTHMA

- The history and physical exam upon presentation in pregnancy should not differ
  - One should have a high suspicion for symptoms including wheezing, chest cough, SOB, chest tightness, and temporal relationship to allergens, exercise, and infection
    - Notably, use of prostaglandins (carboprost) for labor induction/postpartum hemorrhage, OR indomethacin in ASA-sensitive patients can also cause bronchospasm
  - Wheezing upon auscultation supports the diagnosis (but is not mandatory)
- Exacerbations in patients with well-controlled asthma may be due to discontinuation of medications out of fear of negative pregnancy outcomes
  - All asthma meds are category B or C, thus counseling regarding medication safety during pregnancy is paramount. Keeping mommy safe can help keep baby safe!
- Diagnosis can be confirmed by demonstrating reversible airway obstruction
  - Ideally, you will see a >12-15% increase in FEV_1 after bronchodilator administration
- DDx includes: COPD, CHF, PE, laryngeal or vocal cord dysfunction, and mechanical air obstruction

EFFECT OF PREGNANCY ON ASTHMA

- Fetal oxygenation:
  - Fetal arterial pO_2 is much lower than maternal PaO_2 at baseline
  - However, Fetal Hgb has stronger O_2 binding and is therefore able to maintain adequate O_2 saturation
  - Thus, fetus is adaptable to slight variation in maternal PaO_2
- Undertreated asthma is associated with multiple maternal and fetal complications during pregnancy, however, adequately treated asthma is NOT associated with a significant increase in adverse perinatal outcomes

Maternal Complications	Fetal Complications
• **Miscarriage**	• **C-section delivery**
• **Antepartum hemorrhage**	• **Perinatal mortality**
• **Postpartum hemorrhage**	• **Preterm delivery**
• **Anemia**	• **Low birth weight**
• **Preeclampsia**	

MANAGEMENT

- Monitoring lung function can help differentiate between physiologic sensation of dyspnea during pregnancy and asthma exacerbation
  - Look at SPO_2 via pulse oximetry for signs of hypoxia
  - Further, in true exacerbations, peak flows (PEFR) and FEV_1 will decrease
    - Baseline peak flows during pregnancy aren't different than pre-pregnancy levels and it is imperative that patients know their baseline peak flows with which to compare during potential exacerbations
      - Baseline normal range for 20-40 y/o range from 370-529 L/min (can look online for specific age-based values)
- Smoking cessation!
- Optimize environmental triggers or allergens
- Pharmacologic management (next slide)

OVERVIEW OF MAINTENANCE MGMT

STEP 1	STEP 2	STEP 3-4	STEP 5-6
SABA PRN	**Low-dose ICS** *Alternates: cromolyn, or LTRA, or theophylline*	**Low-dose OR Med-dose ICS + LABA** *Alternate: low-to-med dose ICS + LTRA or theophylline*	**High-dose ICS + LABA + oral steroid (if needed)** *Alternate: switch LABA with theophylline*
MILD INTERMITTENT	MILD PERSISTENT	MOD PERSISTENT	SEVERE PERSISTENT

~~See Family Med Asthma Flames for even more details on pharmacologic mgmt~~

MANAGEMENT

PHARMACOLOGY

- Short-acting beta agonist (SABA) (Albuterol):
  - Relaxes bronchiolar smooth muscle
    - Recall: beta agonists (ex. terbutaline) also relax uterine smooth muscle, thus they can be used as tocolytics for preterm labor
      - However, in general, benefits of inhaled SABAs in asthmatics far outweigh risks
  - Delivered through metered-dose inhaler (MDI)
- Long-acting beta agonist (LABA) (Salmeterol):
  - Minimal human data but animal safety data is reassuring
- Epinephrine:
  - Not recommended in pregnancy except in emergent anaphylaxis d/t compromising uterine blood flow

Drug	Category
Albuterol	C
Salmeterol	C
Theophylline	C
Budesonide	B
Beclomethasone	B
Inhaled ipratropium	B
Zafrilukast	B
Montelukast	B
Zileuton	C
Omalizumab	B
Cromolyn Sodium	B

MANAGEMENT

PHARMACOLOGY

- Inhaled corticosteroids (ICS):
  - Anti-inflammatory agent that decreases edema and secretions in bronchioles
  - Inhaled glucocorticoids have lower doses and systemic effects than oral, strong safety profile during pregnancy
  - Budenoside and beclamethasone most recommended
- Systemic corticosteroids:
  - Increased risk of cleft lip with first trimester use
  - Associated with gestational diabetes, preeclampsia, preterm delivery, and low birth weight
  - Oral/systemic glucocorticoids typically reserved for acute exacerbation, not long term control so benefits outweigh risks

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Salmeterol	C
Theophylline	C
Budesonide	B
Beclomethasone	B
Inhaled ipratropium	B
Zafrilukast	B
Montelukast	B
Zileuton	C
Omalizumab	B
Cromolyn Sodium	B

MANAGEMENT

PHARMACOLOGY

- Anticholinergic medications (Ipratropium):
  - Inhibit vagally-mediated reflexes by antagonizing Ach action; prevents increase in intracellular Ca^{2+} that is caused by interaction of Ach w/ muscarinic-r on bronchial smooth muscle
  - Inhaled formulation of ipratropium has low systemic effects and low risk to fetus, safe during pregnancy
- Cromolyn: Mast cell stabilizer
  - Inhibits release of histamine, leukotrienes, and slow-reacting substance of anaphylaxis form mast cells by inhibiting degranulation following exposure to reactive antigen

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MANAGEMENT

PHARMACOLOGY

- Leukotriene receptor antagonists (LTRA):
  - Montelukast:
    - Blocks binding of leukotriene D4 (LTD4) to its receptor; alters pathophysiology associated w/ inflammatory processes that contribute to asthma
    - Safe during pregnancy, but not protective over certain asthma-related pregnancy complications including low birth weight
    - Best used as adjunctive adjunct to glucocorticoid therapy or other stronger maintenance therapy
  - Zileuton:
    - Inhibits 5-lipoxygenase which inhibits formation of LTB4, LTC4, LTD4, and LTE4
    - Insufficient human data but animal studies *not reassuring;* thus not recommended yet

Drug	Category
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Salmeterol	C
Theophylline	C
Budesonide	B
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Inhaled ipratropium	B
Zafrilukast	B
Montelukast	B
Zileuton	C
Omalizumab	B
Cromolyn Sodium	B

MANAGEMENT

PHARMACOLOGY

- Omalizumab:
  - Monoclonal antibody that selectively binds IgE and inhibits binding to IgE-r on surface of mast cells and basophils
- Theophylline:
  - Relaxes smooth muscles of respiratory tract and suppresses response to reactive stimuli
  - Highly susceptible to alterations in drug metabolism and protein binding caused by physiologic changes during pregnancy; thus has to be monitored with serial serum levels (target: 5-12 ug/mL)
  - Easily crosses placenta, fetal drug levels similar to maternal
  - May increase cAMP by inhibiting PDE III and PDE IV which may cause uterine relaxation

Drug	Category
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MANAGEMENT (MOD-TO-SEVERE)

- Antepartum testing:
  - Serial growth ultrasounds starting at 32 weeks
  - Twice weekly NSTs starting at 32-34 weeks
- Baseline evaluations:
  - Baseline PEFR and/or spirometry at 1st visit and trend throughout pregnancy
  - Consider baseline pre-eclampsia labs with which to compare later on if concern develops
    - Hgb, Plt, AST, ALT, Cr, Urine random protein:creatinine ratio
- Flu vaccine!
- Labor:
  - Do not discontinue asthma medications
  - If have taken systemic corticosteroids this pregnancy, consider 100 mg hydrocortisone IV q8h until 24 hours post-partum to prevent adrenal crisis

MANAGEMENT
ACUTE EXACERBATIONS

Mild-to-Mod: FEV1 or PEFR ≥ 50%
- Oxygen if SaO2 < 90%
- Inhaled SABA nebulizer/inhaler
- Oral systemic glucocorticoids

Severe: FEV1 or PEFR < 50%
- Oxygen if SaO2 < 90%
- High dose inhaled SABA nebulizer/inhaler
- Oral systemic glucocorticoids

Impending or actual respiratory arrest:
- Intubation/mechanical ventilation
- Nebulized SABA and ipratropium
- IV glucocorticoids

- Do not forget to check for fetal well-being, inclusive of a NST or continuous fetal monitoring if fetus is viable
- Discharge criteria:
  - Sustained FEV1/PEFR > 70% for > 60 minutes, no distress, reassuring fetal status
  - If < 50% = remain inpatient
  - If 50-70%, individualize decision
- Discharge mgmt:
  - Continue ICS + SABA PRN
  - Oral corticosteroids (40–60 mg split in 1-2 doses/day for 3–10 days)
  - F/u appt in <5 days

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