Asthma and Pregnancy

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Severe Acute Maternal Morbidity (SAMM)

- "near miss" case means a woman with organ dysfunction or failure who would have died had it not been that luck or good care was on her side
- There are nearly five times as many SAMMs as maternal deaths

- Sun Feb 26 16:19:42 2012 Science in Africa publication
Political- Reality

- One in five women of reproductive age had no health insurance, increasing their likelihood of entering pregnancy with unmanaged diseases
- Late or no prenatal care
- Only going to get worse with cut backs in Medicaid and Medicaid expansion

Chance to alter the fatal outcome

- Asthma complicates 4-8% of pregnancies
- Prevalence and morbidity rates are increasing although the mortality rate has decreased
- Insight into the pathogenesis has changed recognition
  - airway inflammation occurs in almost all cases
Unstable Asthmatic Presents to ED or L+D

“This situation does not call for freaking out!”

Very Quick Review Physiology

- Gravid women are designed to tolerate birth, blood loss, and breastfeeding
- Every organ system changes
- People at the bedside must know “normal” for pregnant women to protect and advocate for them
- When our patient’s CRASH they CRASH hard and FAST!

Hemodynamic Profiles for Nonpregnant & Pregnant Patients in the 3rd Trimester

<table>
<thead>
<tr>
<th></th>
<th>Nonpregnant</th>
<th>Pregnant</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD (L/min)</td>
<td>4.3 ± 0.9</td>
<td>6.2 ± 1.0</td>
<td>+43%</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>71 ± 10</td>
<td>83 ± 10</td>
<td>+17%</td>
</tr>
<tr>
<td>SVR (dyne-sec-cm⁻¹)</td>
<td>1530 ± 520</td>
<td>1210 ± 266</td>
<td>-21%</td>
</tr>
<tr>
<td>PVR (dyne-sec-cm⁻¹)</td>
<td>119 ± 47</td>
<td>78 ± 22</td>
<td>-34%</td>
</tr>
<tr>
<td>CVP (mm Hg)</td>
<td>3.7 ± 2.6</td>
<td>3.6 ± 2.5</td>
<td>NS</td>
</tr>
<tr>
<td>COP (mm Hg)</td>
<td>20.8 ± 1.0</td>
<td>18.0 ± 1.5</td>
<td>-14%</td>
</tr>
<tr>
<td>PCWP (mm Hg)</td>
<td>6.3 ± 2.1</td>
<td>7.5 ± 1.8</td>
<td>NS</td>
</tr>
<tr>
<td>COP-PCWP</td>
<td>14.5 ± 2.5</td>
<td>10.5 ± 2.7</td>
<td>-28%</td>
</tr>
</tbody>
</table>

Clark SL, AJOG 1989
Hemodynamic Parameters

<table>
<thead>
<tr>
<th></th>
<th>3rd trimester values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac output</td>
<td>↑ 30-50% 6.0-8.0 L/min</td>
</tr>
<tr>
<td>SVR</td>
<td>↓ 10-15% 1000-1400 dynes/sec/cm -5</td>
</tr>
<tr>
<td>Mean BP</td>
<td>↓ 84-96 mm Hg</td>
</tr>
<tr>
<td>Heart rate</td>
<td>↑ 20% 75-95 beats/min</td>
</tr>
<tr>
<td>PVR</td>
<td>↓ 55-100 dynes/sec/cm -5</td>
</tr>
</tbody>
</table>

- Progressive change over pregnancy leading up to delivery
- Biggest changes occur postpartum
- Cesarean does not prevent changes from occurring and rarely is indicated for medical indications

Respiratory Variables

<table>
<thead>
<tr>
<th></th>
<th>Changes during pregnancy</th>
<th>Third Trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tidal volume</td>
<td>↑ 40% 700 ml</td>
<td></td>
</tr>
<tr>
<td>FRC</td>
<td>↓ 20-25% 1350 ml</td>
<td></td>
</tr>
<tr>
<td>Minute ventilation</td>
<td>↑ 40% 30-50%</td>
<td></td>
</tr>
<tr>
<td>SvO2</td>
<td>Normal 75%</td>
<td></td>
</tr>
</tbody>
</table>

- Dyspnea is normal, but....
- Patients become hypoxic rapidly
- Respiratory alkalosis is physiologic
- Intubation is more difficult

Functional Changes in Pregnancy

- Enlarging Uterus elevates the diaphragm about 4 cm

- Physiologic Changes:
  - Increased Tidal Volume
  - Decreased Functional Residual Capacity
  - Minute Ventilation Increased
  - Physiologic Dead space increased

- No A:
  - Peak Expiratory Flow Rate (PEFR)
  - Forced Expiratory Volume in 1 sec (FEV1)
  - Forced Vital Capacity

- Physiologic dyspnea of pregnancy common: shortness of breath with mild exertion
Respiratory Variables Blood Gas

<table>
<thead>
<tr>
<th>Changes during Third Trimester</th>
<th>pH</th>
<th>pCO₂</th>
<th>P0₂</th>
<th>HC03</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>unchanged</td>
<td>↓ 27-32mmHg</td>
<td>↑ 100-108 mmHg</td>
<td>↓ 18-21 meq/l</td>
</tr>
</tbody>
</table>

Beware a pCO₂ of 40 is ominous

Asthma Diagnosis

- Diagnosis = symptoms + spirometry results
- Symptoms: paroxysmal, persistent breathlessness, chest tightness, cough, sputum production
- Improved FEV1 after admin of B2 agonist and increased sensitivity to mthacholin
  - Test not usually performed in pregnancy

Classification of Asthma Control in Pregnant Patients

<table>
<thead>
<tr>
<th>Sign and Symptom</th>
<th>Well Controlled</th>
<th>Not Well Controlled</th>
<th>Very Poorly Controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency/Short Acting B Agonist Use</td>
<td>&lt;= 2 days per week</td>
<td>&gt;2 days, not daily</td>
<td>Throughout the day</td>
</tr>
<tr>
<td>Nighttime awakening</td>
<td>&lt;= 2 times per month</td>
<td>&gt;2 times per month</td>
<td>&gt;1 time per week</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
<td>&gt;2 times per month</td>
<td>&gt;1 time per week</td>
</tr>
<tr>
<td>FEV1 or peak flow (percent predicted/personal best)</td>
<td>&gt;80%</td>
<td>&gt;80%</td>
<td>&gt;60%</td>
</tr>
</tbody>
</table>
Effects of Asthma on Pregnancy

• Large, prospective study of pregnant women

<table>
<thead>
<tr>
<th></th>
<th>Exacerbation Rate</th>
<th>Hospitalization Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild Asthma</td>
<td>12.6%</td>
<td>2.3%</td>
</tr>
<tr>
<td>Mod Asthma</td>
<td>25.7%</td>
<td>6.8%</td>
</tr>
<tr>
<td>Severe Asthma</td>
<td>51.9%</td>
<td>26.9%</td>
</tr>
</tbody>
</table>

- 23% improved in pregnancy, 30% became worse in pregnancy
- Concluded that pregnant women with mild or even well-controlled asthma should be monitored with PEFR and FEV1 testing during pregnancy

Effect of Asthma on Pregnancy Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Maternal</th>
<th>Perinatal</th>
<th>Fetal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antepartum and PP hemorrhage</td>
<td>Placenta Pevia</td>
<td>Death</td>
<td></td>
</tr>
<tr>
<td>Cesarean</td>
<td>Placental abruption</td>
<td>Hospitalization</td>
<td></td>
</tr>
<tr>
<td>GDM</td>
<td>Premature rupture membranes</td>
<td>Low birth weight</td>
<td></td>
</tr>
<tr>
<td>Gestational hypertension</td>
<td>Small gestational age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>Cleft lip/palate</td>
<td></td>
<td></td>
</tr>
</tbody>
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Effects of Asthma on Pregnancy

Results of 8 Prospective Studies:

• Mild or Moderate asthma can have excellent maternal and perinatal outcomes
• Suboptimal control is associated with increased risk to mother and infant
• Lower FEV1 values during pregnancy are associated with increased risk of low birth weight and prematurity
Management Approaches: Goals

- Maintain adequate oxygenation of the fetus by prevention of hypoxic episodes in the mother
- Minimal or no maternal symptoms day or night
- Minimal or no exacerbations
- No limitations of activities
- Maintenance of normal or near normal pulmonary function
- Minimal use of B2 agonists
- Minimal or no adverse side effects from medications

Components of Effective Asthma Therapy in Pregnancy

- Monthly assessment of asthma control using objective measures
  - Structure asthma history using a validated questionnaire
    - ACQ, ACT, GINA
  - Monitoring lung functions by spirometry or peak expiratory flow
  - Fetal monitoring after 32 weeks

Treatment of Comorbid Conditions

- Rhinitis
- GERD
- Depression
- Allergy
Four Integral Components:
1) Objective assessment
2) Trigger avoidance
3) Patient Education
4) Pharmacologic Therapy

Objective Assessment
- Subjective measures are insensitive and inaccurate
- FEV1 value after maximal inspiration is the single best measure of pulmonary function
- A mean FEV1 < 80% of predicted value has been significantly associated with:
  - increased preterm delivery at less than 32 weeks and less than 37 weeks
  - Birthweight less than 2500g

Peak Flows
- Patients with persistent asthma should be evaluated at least monthly
- Moderate/Severe asthmatics should be evaluated daily
- Typical PEFR= 380 to 550 L/min
- Establish personal best then calculate individual PEFR zones
  - Green= 80% of personal best
  - Yellow=50 to 80% of personal best
  - Red= less than 50% of personal best
Four Integral Components:
1) Objective assessment
2) Trigger avoidance
3) Patient Education
4) Pharmacologic Therapy

Avoidance of Environmental Triggers
- Cigarette smoking
- Animal allergens
- House dust mites
- Cockroaches
- Indoor mold
- Fireplaces
- Perfumes
- Cleaning agents
- Aerosol sprays
- Pollen
- Air pollution
- Food additives

Avoiding and Controlling Asthma Triggers
- Limit adverse environmental exposures
- 75% to 85% of patient with asthma have positive skin tests to common allergens
- Physical activity
Four Integral Components:
1) Objective assessment
2) Trigger avoidance
3) Patient Education
4) Pharmacologic Therapy

Patient Education
• Preconception education
• Inhaler technique
• Written asthma action plan
• Specifically address teratogen concerns and risks of medication discontinuation

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Four Integral Components:
1) Objective assessment
2) Trigger avoidance
3) Patient Education
4) Pharmacologic Therapy
Pharmacologic Therapy

Goals:

• Relieve bronchospasm
• Protect the airway from irritant stimuli
• Mitigate pulmonary and inflammatory response to allergen exposure
• Improve pulmonary function
• Reduce airway hyperresponsiveness

A Stepwise Approach

• Uses least amount of drug intervention necessary to control severity of a patient’s asthma
• Safer for pregnant women to treated with asthma medication than it is for them to have asthma symptoms and exacerbations
• Emphasis is on treatment of airway inflammation to decrease hyperresponsiveness and prevent symptoms

Asthma Medical Management in Pregnancy

<table>
<thead>
<tr>
<th>Severity Level</th>
<th>Medication Type</th>
<th>Daily Dose</th>
<th>Route</th>
<th>Early Pregnancy</th>
<th>Late Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild exacerbation</td>
<td>Long-Acting Betaagonist (LABA)</td>
<td>200 mcg qd</td>
<td>Inh.</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Severe exacerbation</td>
<td>Long-Acting Betaagonist (LABA) + Inhaled Corticosteroids (ICS)</td>
<td>200 mcg qd + 500 mcg qd</td>
<td>Inh.</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

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Inhaled Corticosteroids
• Preferred management for all levels of persistent asthma during pregnancy
• Prospective, observational study of 504 pregnant women with asthma
• 177 not treated with budesonide (Pulmicort) or beclomethasone (Qvar)
• 17% rate of acute exacerbations in control group
• Only 4% rate in treatment group

Inhaled Corticosteroids
• NAEPP Working Group reviewed 10 studies including 6113 patients who took inhaled corticosteroids during pregnancy for asthma
• Rates of congenital malformations not increased
• Rates of adverse perinatal outcomes not increased

Inhaled B₂ -Agonists
• Recommended for all degrees of asthma during pregnancy
• MOA: smooth muscle relaxation
• Side effects: tremor, tachycardia, palpitations
• Safety: no relationship with adverse pregnancy outcomes
**Cromolyn**
- MOA: blocks early and late phases of pulmonary response to an allergen challenge
- Prevents the development of airway hyperresponsiveness
- Slower onset than inhaled corticosteroids
- Less effective in reducing objective and subjective manifestations
- Safe in pregnancy

**Theophylline**
- Alternative treatment for mild, persistent asthma
- Adjunct treatment for mod and severe
- MOA: anti-inflammatory actions
- Side effects: insomnia, heartburn, palpitations and nausea
- High dose side effects: jitteriness, tachycardia and vomiting
- Dosing: 5-12 Ug/ml in pregnancy
- Interactions: cimetidine and erythromycin will increase serum levels
- Advantages: long duration of action 10-12 hrs useful for nocturnal asthma
- Safety: considered safe in pregnancy

**Leukotriene Mediators**
- MOA: inhibit pathway of arachidonic acid metabolites which have been implicated in transducing bronchospasm, mucus secretion and increased vascular permeability
- Safety: Category B
- Minimal data available
- Alternative treatment for mild persistent asthma
- Adjunctive therapy in mod or severe asthma
Oral Corticosteroids

- Associated with three fold risk of orofacial cleft
- Increased incidence of preeclampsia, preterm delivery, low birth weight
- Prospective study found deficit of 200 g in birth weight compared to controls and those exclusively treated with beta 2 agonists
- NAEPP recommends use for long-term management of severe asthma or exacerbations

Additional Asthma Therapies

<table>
<thead>
<tr>
<th>Drug category</th>
<th>Drug</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukotriene receptor agonists</td>
<td>Montelukast</td>
<td>Most safety data available for montelukast</td>
</tr>
<tr>
<td></td>
<td>Zafirlukast</td>
<td></td>
</tr>
<tr>
<td>Xanthine derivative</td>
<td>Theophylline</td>
<td>Monitor serum levels for toxicity</td>
</tr>
<tr>
<td>Monoclonal antibody</td>
<td>Omalizumab</td>
<td>Should not be started AP due to risk of anaphylaxis</td>
</tr>
<tr>
<td>Allergen Immunotherapy</td>
<td>Subc subl</td>
<td>Should not be started AP due to risk of anaphylaxis except in Hymenoptera venom sensitivity</td>
</tr>
<tr>
<td></td>
<td>venom</td>
<td></td>
</tr>
<tr>
<td>5-lipoxygenase inhibitor</td>
<td>Zileuton</td>
<td>Potential teratogen don't use</td>
</tr>
</tbody>
</table>

Hospital Management

- Initial Assessment
  - Good Response
  - Incomplete Response
  - Poor Response
    - Impending or Actual Respiratory Arrest
Hospital Management of Exacerbation

Initial Assessment:
- H&P (auscultation, use of accessory muscles, heart rate, RR, assess ox saturation)
- Abnormal ABG: PaCO2 > 35 and PaO2 < 70
- Fetal assessment: FHT, BPP
- Severe Exacerbation: high dose nebulizer treatment q 20 mins x 1 hour + ipratropium bromide + systemic steroid
- O2 admin with goal of sat > 95%
- Repeat albuterol q 60 mins for 1-3 hrs provided there is improvement

Criteria for Home Discharge
- Greatly improved symptoms and PE findings
- Ability to walk out of ED without obvious distress
- PEFR/FEV1 > 70% baseline
- Reassuring fetal status
- Good follow-up and access to ED in case of relapse
- Willingness to follow-up in 2-4 days

Incomplete Response
- FEV1 or PEFR 70% of normal or greater
- Symptoms are mild or moderate
- Continue fetal assessment until patient is stabilized
- Monitor PEFR, ox saturation and pulse
- Continue nebulizer treatments and oxygen
- Administer ipratropium bromide
- Administer a systemic corticosteroid (oral or IV)
- Decision to hospitalize is individualized
Criteria for Hospital Admission

- Inadequate response to ED therapy
- \(P_{O2} < 70 \text{ mm HG}\)
- Concerning fetal status
  - Decreased fetal movement
  - Non-reassuring fetal tracing
  - Contractions
- Multiple medication use
- A protracted course with poor response to outpatient therapy
- History of severe asthma requiring intubation/ICU
- Inadequate home conditions and transport/access to ED care

Criteria for ICU Admission

- Altered level of consciousness
- Poor air flow
- Signs of fatigue
- Downhill course
- Need for Mechanical Ventilation
- \(PEFR/FEV1 < 25\% \text{ of predicted or pCO2 } > 35\text{ mm Hg}\)

Mechanical Ventilation

- < 1\% of asthmatics require Mechanical Ventilation
- Early and expert intubation and MV
- Difficult to ventilate
  - Extremely high peak airway pressures
  - Barotraumas
  - Hemodynamic impairment
  - Mucous plugging
  - Atelectasis
  - Secondary pneumonia
**Mechanical Ventilation**

- Typical ventilator settings:
  - Stacked breaths
  - Increased airway pressures
- Prolonged expiratory time ventilation strategy
  - Low tidal volume (6-8 ml/kg)
  - RR (8-12 breaths/min)
  - High inspiratory flow rate (up to 100 l/min)

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**Labor and Delivery Management**

- Continue asthma medications
- Consider PEFRs on admission and at 12 hour intervals
- Administer stress dose steroids if systemic steroids have been used in the previous 4 weeks
- Lumbar anesthesia reduces oxygen consumption and minute ventilation in labor

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**Labor and Delivery Management**

- Prostaglandin F2-alpha can cause bronchoconstriction, E2 or E1 are considered safe
- Hemabate and Methergine can cause bronchospasm
- Magnesium is a bronchodilator
- Indomethacin can cause bronchoconstriction in the aspirin sensitive patient
Breastfeeding
• Only small amounts of asthma medicines enter breast milk
• Theophylline may cause toxic effects in the neonate including vomiting, feeding difficulties, jitteriness and cardiac arrhythmias

Take Home Points
• Mild Asthma in pregnancy is more like moderate persistent asthma outside of pregnancy when considering exacerbation rates

• Follow a stepwise approach to treatment
• “It is safer for the pregnant woman with asthma to be treated with asthma medications than it is for them to have asthma symptoms and exacerbations” –NAEPP

Maternal Codes
Evaluating Clinician
Anesthesiologist
Primary Obstetric Provider
Nurse Anesthetist
Patient
Resuscitation Team
Emergency Physician
Nurse Midwife
Hospitalist
Intensivist
Treatment Algorithm

- Circulation
- Airway
- Breathing
- Defibrillate
- Extract Fetus

IMMEDIATE ACTIONS:

- Call Obstetric Code
- Call for Neonatal team (if viable pregnancy)
- Begin BLS Immediately
- Get Adult code cart & backboard
- Begin preparation for cesarean
- Assign a staff as a timekeeper/documentation

BEGIN ACLS ALGORITHMS - PLACE AED
Perimortem Cesarean

• Rationale
  – 20% of maternal blood flow goes to uterus at term
  – Goal of improving compression of the IVC by the gravid uterus
  – Decrease O2 demand
  – Improve pulmonary mechanics
  – Review of 60 cases showed definite benefit in 31% of cases and no worsening of maternal survival in any cases
  – May improve maternal cardiac output 30 – 80%
Extra slides for your review