Pulmonary Disease in Pregnancy

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• No financial interests to disclose.
Objectives

• Physiologic changes in pregnancy –
  – Pulmonary
  – ABGs, etc

• Asthma overview
  – Diagnosis
  – Classification
  – Management
Case 1

• 28yo P0
• 12 weeks
• Hx of asthma-
• Takes rescue inhaler daily
• No maintenance medication
• Management?
Case 2

• 30 yo P4004 at 20 weeks’ gestation, healthy, presents to ED for altered mental status, somnolent, HA, dizziness, palpitations, n/v. Husband reports pt was sleeping in back room of house with space heaters.

• Diagnosis/Treatment?
Physiologic Changes

• Uterus enlarges, viscera are pushed up

• Chest wall
  – Diaphragm is elevated (4cm)
  – Increase in circumference (6cm)
  – Widening of costal angles (70 to 104 degrees)
  – Increase in diaphragmatic excursion (1.5cm)

• Occur before increases of uterine size, maternal body weight, or intraabdominal pressure

• Respire for the fetus
Respiratory physiology in pregnancy

- Upper airways
  - Mucosal edema
  - Capillary engorgement
  - Edema in preeclamptics, patients that have been aggressively hydrated
Why Pregnant Women Breathe More

• Progesterone induced hyperventilation
  – Serum levels increase in pregnancy
    • 25ng/mL at 6 weeks; term - 150ng/mL
  – Stimulates central respiratory center
    • Increased sensitivity to CO2
    • Estrogen increases central expression of progesterone receptors
  – Net = increased ventilatory drive

• Acute asthma ‘superimposes’ extra hyperventilation
  • More severe compromise during pregnancy vs nonpregnant state
Oxygen dissociation

- Right shift causes decreased maternal affinity for O2 (increased levels of 2,3-DPG)
- HbF is unable to react to 2,3-DPG, and so maintains high affinity for O2 despite relative acidemia
Respiratory Musculature

• Respiratory muscle function is unchanged
  – Maximal inspiratory and expiratory pressures are unchanged
Lung Volumes
Lung Volumes

- **Respiratory rate (# breaths/minute)** – no change
- **Total lung capacity** – total amount of volume you can breathe in after max inspiration
  - decreased
- **Vital capacity** – expired vol with maximal exhalation - NC
- **Residual volume** – what is left after maximal exhalation
  - volume in lungs after VC; decreased by 20%
- **FRC** – functional residual capacity – volume remaining after normal expiration (take normal breath out – how much vol is left in lungs)
  - Decreased 20%, by 300-500 mL – due to elevation of diaphragm
  - Changing from sitting to supine at term causes another 25% decrease in FRC
    - may increase closure of small airways especially in obese patients in the supine or lithotomy position
- **ERV** – expiratory reserve volume – (FRC – RV)
  - (Vol left after normal breath) – (Vol left after maximal breath)
Other variables

- Airway function – unchanged
- Diffusing capacity – unchanged
- Oxygen delivery – dependent on Hb
  - $O_2$ delivery = $CO \times CaO_2 \times 10$
  - $CaO_2 = (Hgb \times 1.34 \times SaO_2) + (PaO_2 \times 0.0031)$
  - $CaO_2$ is thus much more dependant on Hgb function than diffusion of $O_2$ into serum
  - $O_2$ delivery can be significantly affected by maternal anemia or CO poisoning
  - Physiologic anemia of pregnancy is compensated by a 50% increase in CO (increases in both HR and SV)
Minute Ventilation is Increased

- Minute ventilation – RR x TV
  - Increases 40% to 100-200cc during early pregnancy and remains constant

- More ventilation at the expense of reserves
  - Increased AP diameter expansion
    - Chest circumference increases 2cm
    - Diaphragm excursion not impaired, rather increases
  - Use up FRC, VC
Respiratory physiology in pregnancy

• Residual volume
  – volume of air remaining in the lungs after maximal expiration
  – decreases 20% due to elevation of diaphragm

• Functional residual capacity (volume of air in lungs at resting expiratory level)
  – decreases 20% due to elevation of diaphragm
  – decreases 300-500mL
  – changing from sitting to supine at term causes another 25% decrease in FRC
    • may increase closure of small airways especially in obese patients in the supine or lithotomy position
Pathophysiologic Implications

- Mom is able to hold her breath less
  - 1 vs 2 lung example

- Decreased FRC
  - Closing capacity – amount of volume that has to be behind to keep small airways open - diminished

- Develop hypoxemia quicker than when not pregnant (at greater risk of hypoxemia)

- Pulmonary insults are tolerated less well
**ABG Changes in Pregnancy**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nonpregnant</th>
<th>Pregnant</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.35-7.43</td>
<td>7.4-7.47</td>
</tr>
<tr>
<td>pCO2 (mmHg)*</td>
<td>37-40</td>
<td>27-31</td>
</tr>
<tr>
<td>pO2 (mmHg)**</td>
<td>103</td>
<td>101-104</td>
</tr>
<tr>
<td>P(A-a)O2 (mmHg)***</td>
<td>14</td>
<td>20</td>
</tr>
<tr>
<td>HCO3- (mEq/L)</td>
<td>22-26</td>
<td>18-22</td>
</tr>
<tr>
<td>Base deficit (mEq/L)</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

*compensatory increase in renal bicarbonate excretion*

**decreased in supine position and 3rd trimester**

***increased by 6 in supine position and 3rd trimester***
## Blood Gas Interpretation – Pregnant Women

<table>
<thead>
<tr>
<th>pO2</th>
<th>pCO2</th>
<th>pH</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Decreased</td>
<td>Increased</td>
<td>Mild distress, compensated</td>
</tr>
<tr>
<td>Decreased</td>
<td>Decreased</td>
<td>Increased</td>
<td>Moderate distress, compensated</td>
</tr>
<tr>
<td>Decreased</td>
<td>Normal (~27-31)</td>
<td>Normal</td>
<td>Danger – Impaired Ventilation</td>
</tr>
<tr>
<td>Decreased</td>
<td>Increased (&gt;40)</td>
<td>Decreased</td>
<td>Respiratory Failure</td>
</tr>
</tbody>
</table>
CXR changes in pregnancy

• Apparent cardiomegaly (enlarged transverse diameter)
• Enlarged left atrium (lateral views)
• Increased vascular markings
• Straightening of left heart border
• Postpartum pleural effusion (right sided)
CXR
Case

- 34 yo P0, admitted for preeclampsia
  - IVF pregnancy
- HD #3, developed progressive dyspnea, crackles on physical exam, oxygen requirements
  - CXR revealed bilateral pleural effusions
- Fluid restriction, diuretics (Lasix 20mgIV), delivery, seizure prophylaxis
CXR of pulmonary edema
Pulmonary Edema in Preeclampsia

- **Management**
  - Oxygen, Fluid Restriction, Semi-Fowler
  - Accurate intake/output
  - If Fluid Overload, then Lasix, Increasing Doses as Needed
  - Consider PA Catheter: Fluid Overload vs. LV Dysfunction vs. Nonhydrostatic Pulmonary Edema
Indications for PA Catheter in Hypertensive Disease

- Severe preeclampsia with refractory oliguria or pulmonary edema
- Ineffective IV antihypertensive therapy
- Intraoperative or intrapartum cardiac failure
Pulmonary Edema in Preeclampsia – 3 subsets

- Management
  - Intravascular volume depletion (oliguria), low PCWP, high CO, high SVR, low CVP –
    - fluids
  - Renal Vasoconstriction (High PCWP, Normal CO and SVR, uroconcentration):
    - Dopamine – 1-5µg/kg/min; furosemide
  - LV Dysfunction/Failure with Vasospasm (high PCWP, high SVR, low CO <5 L/min) :
    - Needs Afterload Reduction (Sodium nitroprusside 0.25-0.5µg/kg/min IV infusion)
    - Volume Restriction
    - Diuretics (max acute dose of furosemide is 120mg, start with 20-40mg)
  - Mechanical Ventilation for Respiratory Failure (If still Pregnant, Intubate Early rather than Late)
Asthma

• 4-8% of all pregnancies
• Prevalence and morbidity increasing
• Mortality decreasing

• Classification
• Step therapy
Pathophysiology

- Inflammation
- Bronchoconstriction
Diagnosis

• Symptoms (cough, dyspnea, wheezing)
• Demonstration of airway obstruction on spirometry that is partially reversible with a bronchodilator (>12% increase of FEV1 after bronchodilator)

• DDX – Dyspnea of pregnancy, GERD, bronchitis, postnasal drip (allergies)
Pulmonary function testing

• Peak expiratory flow rate (PEFR) – L/min

• Forced expiratory volume in the first second of expiration (FEV1) – L in 1st sec
Individualized PEFR zones

- Establish ‘personal best’ PEFR then determine zone based on the following:
  - Green - >80% of personal best PEFR
  - Yellow – 50-80% of personal best PEFR
  - Red - <50% of personal best PEFR

- Typical PEFR = 380-550 L/min
## Classification – 2004 Asthma in Pregnancy Working Group, NAEP, ACOG

<table>
<thead>
<tr>
<th>Asthma Severity* (Control†)</th>
<th>Symptom Frequency</th>
<th>Nighttime Awakening</th>
<th>Interference With Normal Activity</th>
<th>FEV₁ or Peak Flow (Predicted Percentage of Personal Best)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermittent (well controlled)</td>
<td>2 days per week or less</td>
<td>Twice per month or less</td>
<td>None</td>
<td>More than 80%</td>
</tr>
<tr>
<td>Mild persistent (not well controlled)</td>
<td>More than 2 days per week, but not daily</td>
<td>More than twice per month</td>
<td>Minor limitation</td>
<td>More than 80%</td>
</tr>
<tr>
<td>Moderate persistent (not well controlled)</td>
<td>Daily symptoms</td>
<td>More than once per week</td>
<td>Some limitation</td>
<td>60–80%</td>
</tr>
<tr>
<td>Severe persistent (very poorly controlled)</td>
<td>Throughout the day</td>
<td>Four times per week or more</td>
<td>Extremely limited</td>
<td>Less than 60%</td>
</tr>
</tbody>
</table>

Abbreviation: FEV₁, forced expiratory volume in the first second of expiration

*Assess severity for patients who are not taking long-term-control medications.

†Assess control in patients taking long-term-control medications to determine whether step-up therapy, step-down therapy, or no change in therapy is indicated.
Evaluation & Treatment

• H&P, EKG, Echocardiogram if severe, uncontrolled disease, PFTs

• Avoid triggers

• Reflux – H2 blocker, PPI

• Immunoprophylaxis (Allergy shots) – OK in pregnancy if on maintenance dosing

• Step therapy
Limiting Exposure to Asthma Triggers

- Plastic mattress, pillow covers
- Weekly washing of bedding in hot water
- Animal dander control (baths, pets out of bedroom, keep outside)
- Cockroach control
- Avoid tobacco smoke
- Inhibit mite and mold growth by reducing humidity
- Leave when home is vacuumed
- Immuno therapy OK to continue in pregnancy
Risk Factors Of Death From Asthma

- History of sudden severe exacerbations
- Prior intubations
- Prior admission to ICU due to asthma
- >2 hospitalizations per year
- >3 ER visits for asthma
- Hospitalization or ER visit within last 30 days
- Use of > 2 cannisters of beta agonist per month
- Current use of steroids or recent withdrawal from them
- Comorbidity (cardiovascular or COPD)
- Serious psychiatric illness
- Illicit drug use
- Poor perception of air flow or severity
- Low socioeconomic status
- Sensitivity to mold
Pregnancy Outcomes

- Mild and well-controlled moderate asthma
  - Good outcomes
- Severe and poorly controlled asthma
  - PTB
  - CD
  - Preeclampsia
  - Growth restriction
  - Perinatal complications
  - Maternal morbidity and mortality
The Relationship Of Asthma Medication Use To Perinatal Outcomes

Schatz, et al MFMU Network, 2004

- Study relationship of asthma and asthma medications and adverse perinatal outcomes (risk of preeclampsia, preterm deliveries, and lower-birth-weight infants)
- 16 centers, 1994-2000; N = 2123 asthmatic participants
- No relationship between inhaled beta agonists, inhaled corticosteroids, theophylline and adverse perinatal outcomes
- Oral corticosteroid use associated with preterm birth, LBW
  - Related to asthma severity
  - Mechanism unknown
National Asthma Ed and Prevention Program

• ‘Safer for pregnant women to be on asthma medications to control the disease than it is for them to have asthma symptoms and exacerbations…’
Mild Intermittent

- Pregnancy
  - 13% exacerbation rate
  - 2.3% hospitalization rate
- Symptoms <2d/week or <2nights/month
- PEFR ≥80%
- Management –
  - Avoid triggers
  - Albuterol inhaler, prn
  - No maintenance medication needed
  - Severe exacerbations may occur; long asymptomatic periods are common
  - Course of systemic steroids with exacerbation if needed
Mild Persistent

- Pregnancy
  - 13% exacerbation rate
  - 2.3% hospitalization rate
- Symptoms >2d/wk but not daily; Nighttime awakening >2x/month
- PEFR >80%
- Preferred treatment
  - Low dose inhaled corticosteroid
- Alternative
  - Cromolyn sodium inhaler
  - Montelukast sodium - Leukotriene receptor antagonist – 10mg orally daily
Moderate Persistent

- Pregnancy
  - 26% exacerbation rate
  - 7% hospitalization rate
- Symptoms daily or nighttime awakening >1 night/week
- PEFR 60-80%
- Preferred treatment
  - Medium dose inhaled corticosteroid
  - Long acting beta2 agonist
- Alternative
  - Low dose inhaled corticosteroid
  - Leukotriene receptor antagonist
Severe persistent

- Pregnancy
  - 52% exacerbation rate
  - 27% hospitalization rate
- Symptoms continually, daily; >4 nights/week
- PEFR <60%
- Preferred treatment
  - High dose inhaled corticosteroid steroid
  - Long acting beta2 agonist
  - Oral corticosteroids
    - Prednisone 1-2mg/kg/day
    - Vit D/calcium
- Alternative
  - High dose inhaled steroid
Step Therapy Medical Management of Asthma During Pregnancy

**Mild Intermittent Asthma**
- No daily medications, albuterol as needed

**Mild Persistent Asthma**
- Preferred—Low-dose inhaled corticosteroid
- Alternative—Cromolyn, leukotriene receptor antagonist, or theophylline (serum level 5–12 mcg/mL)

**Moderate Persistent Asthma**
- Preferred—Low-dose inhaled corticosteroid and salmeterol or medium-dose inhaled corticosteroid or (if needed) medium-dose inhaled corticosteroid and salmeterol
- Alternative—Low-dose or (if needed) medium-dose inhaled corticosteroid and either leukotriene receptor antagonist or theophylline (serum level 5–12 mcg/mL)

**Severe Persistent Asthma**
- Preferred—High-dose inhaled corticosteroid and salmeterol and (if needed) oral corticosteroid
- Alternative—High-dose inhaled corticosteroid and theophylline (serum level 5–12 mcg/mL) and oral corticosteroid if needed
## Table 2. Comparative Daily Doses for Inhaled Corticosteroids*

<table>
<thead>
<tr>
<th>Corticosteroid</th>
<th>Amount</th>
<th>Low Dose</th>
<th>Medium Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beclomethasone HFA</td>
<td>40 mcg per puff</td>
<td>2–6 puffs</td>
<td>More than 6–12 puffs</td>
<td>More than 12 puffs</td>
</tr>
<tr>
<td></td>
<td>80 mcg per puff</td>
<td>1–3 puffs</td>
<td>More than 3–6 puffs</td>
<td>More than 6 puffs</td>
</tr>
<tr>
<td>Budesonide</td>
<td>200 mcg per inhalation</td>
<td>1–3 puffs</td>
<td>More than 3–6 puffs</td>
<td>More than 6 puffs</td>
</tr>
<tr>
<td>Flunisolide</td>
<td>250 mcg per puff</td>
<td>2–4 puffs</td>
<td>4–8 puffs</td>
<td>More than 8 puffs</td>
</tr>
<tr>
<td>Fluticasone HFA</td>
<td>44 mcg per puff</td>
<td>2–6 puffs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>110 mcg per puff</td>
<td>2 puffs</td>
<td>2–4 puffs</td>
<td>More than 4 puffs</td>
</tr>
<tr>
<td></td>
<td>220 mcg per puff</td>
<td>1–2 puffs</td>
<td></td>
<td>More than 2 puffs</td>
</tr>
<tr>
<td>Fluticasone DPI</td>
<td>50 mcg per inhalation</td>
<td>2–6 puffs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>100 mcg per inhalation</td>
<td>1–3 puffs</td>
<td>3–5 puffs</td>
<td>More than 5 puffs</td>
</tr>
<tr>
<td></td>
<td>250 mcg per inhalation</td>
<td>1 puff</td>
<td>2 puffs</td>
<td>More than 2 puffs</td>
</tr>
<tr>
<td>Mometasone</td>
<td>200 mcg per inhalation</td>
<td>1 puff</td>
<td>2 puffs</td>
<td>More than 2 puffs</td>
</tr>
<tr>
<td>Triamcinolone</td>
<td>75 mcg per puff</td>
<td>4–10 puffs</td>
<td>10–20 puffs</td>
<td>More than 20 puffs</td>
</tr>
</tbody>
</table>

*Total daily puffs is usually divided into a twice-per-day regimen.

Abbreviations: DPI, dry powder inhaler; HFA, hydrofluoralkane

Home Management Of Acute Asthma Exacerbations

• Inhaled albuterol 2-4 puffs, check PEFR in 20 minutes
  - PEFR <80% predicted despite therapy or <60% without therapy
    • Report to ER/LDR
    • OR, Repeat albuterol treatment, check PEFR in 20 minutes
    • If still 50-80% of predicted, report to ER
  - PEFR > 80% predicted
    • Continue inhaled albuterol (2-4 puffs q3-4hr for 6-12hr prn)
  - If decreased FM
    • ER/LDR
ER/LDR Care

- Evaluation – H&P, PEFR, oximetry, fetal monitoring, ABG
- Treatment
  - Albuterol – 3 puffs, repeat every 15-30 minutes
  - IV hydration
  - Oxygen to maintain saturation >95%
- If no wheezing and PEFR or FEV1 >70% baseline, discharge with follow up; ± oral steroid course
- If PEFR or FEV1 >40% but <70% baseline after beta2 agonist
  - ABG
  - IV corticosteroids
  - Admission to hospital
- If oximetry <90%, FEV1<1.0L, or PEFR <100 L/min on presentation
  - ABG, ICU admission
  - Continuous nebulized albuterol
  - IV corticosteroids (methylprednisolone 1.5mg/kg OR hydrocortisone 100mg IV q8hr)
  - Magnesium sulfate 2gm IV
  - Intubation (CO2 >40)
Pregnancy Management

• Daily peak flow measurements – if able to get meter
  – If 20% drop from baseline, evaluate as risk of impending exacerbation is significant

• Maintenance therapy

• Serial growth scans/BPPs if moderate or severe
Vaccinations

• Influenza – recommended
• Pneumococcal vaccination
  – Immunocompromised
  – HIV +
  – Smoker
  – Diabetes mellitus
  – Cardiac disease
  – Pulmonary disease
  – Asthma
  – Renal disease
  – Asplenia, sickle cell disease patients
  – 2nd/3rd trimester – PPSV 23

CDC
Williams Obstetrics
Labor and Delivery

- O2 saturation, Peak flows if moderate or severe on admission, q 12 hr
- Give asthma medications while in labor if due for dose
- IV hydration
- Adequate analgesia to reduce chance for bronchospasm
- Chronic steroid use – (intermittent, in last 4-6 weeks)
  - Hydrocortisone 100mg q 8hr during labor and for 24 hrs following delivery to prevent adrenal crisis (NAEP)
- Mode of delivery – vaginal
  - If asthmatic crisis, at term, refractory to medical intervention, expediting delivery could improve the respiratory status and ability to ventilate
- PGE1 and PGE2 – OK (ripening, induction, PPH)
- Carboprost and methylergonovine can cause bronchospasm
- Magnesium sulfate (can act as bronchodilator) is safe in PTL and seizure ppx
- Indomethacin can induce bronchospasm in aspirin sensitive pts
Breast Feeding

• In general only small amounts of meds enter breast milk
  – OK with prednisone, antihistamines, beclomethasone, beta agonists, and cromolyn
  – Theophylline sensitive individuals
    • Toxicity includes vomiting, feeding difficulties, jitteriness, cardiac arrhythmias
Pulmonary Insults are More Likely During Pregnancy and Pregnant Women are More Prone to Respiratory Problems and Failure
Case 1

• 28yo P0
• 12 weeks
• Hx of asthma-
• Takes rescue inhaler daily
• No maintenance medication
• Management? – Inhaled corticosteroid-stepwise tx
Case 2

• 30 yo P4004 at 20 weeks’ gestation, healthy, presents to ED for altered mental status, somnolent, HA, dizziness, palpitations, n/v. Husband reports pt was sleeping in back room of house with space heaters.

• Diagnosis/Treatment?
Case

• 30 yo P4004 at 20 weeks’ gestation, healthy, presents to ED for altered mental status, somnolent, HA, dizziness, palpitations, n/v. Husband reports pt was sleeping in back room of house with space heaters. Diagnosis/Treatment?

• A- CO\textsuperscript{−} poisoning, plasma exchange
• B- CO\textsuperscript{−} poisoning, 100% O2 by face mask, possible hyperbaric treatments
• C- CO\textsuperscript{−} poisoning, dialysis
• D- CO\textsuperscript{−} poisoning, blood transfusion
Carbon Monoxide poisoning

- Carboxyhemoglobin level
  - 5-20% - Maternal symptoms
  - 30-50% - CV collapse
  - >50% fatal

- Hb F has higher affinity for CO HB, fetal concentration 10-15% higher than maternal

- T1/2 – 2hr (mother), 7hr (fetus)

- Tx – Oxygen 100%, hyperbaric treatment if COHb >15-20%
Conclusions

• FRC decreased by 20%
• PCO2 > 40, respiratory distress, impending failure in pregnant women
• Asthma classes
• Step therapy
• ER if FEV1 <80%, Admit if FEV1 <70%
• Avoid hemabate
End 9-13-17

• ??
Extra slides

- In resident review
- Facts/Questions
- Cases
- CF
- TB
- Pulmonary edema
- CO poisoning
Case 3

• 30 yo P0000
• History of cystic fibrosis
• 12 weeks
• Evaluation/management?
Cystic Fibrosis
EFFECTS OF CYSTIC FIBROSIS
Multisystem disease

- Infection of airways
- Severe hepatobiliary disease (5–10% of cases)
- Pancreatic exocrine insufficiency
- Meconium ileus at birth (15–20% of cases)
- Sweat chloride value usually 90–110 mmol/liter, sometimes 60–90 mmol/liter
- Obstructive azoospermia
- Adequate pancreatic exocrine function (usually); pancreatitis (5–20% of cases)
- Sweat chloride value usually 60–90 mmol/liter; sometimes normal (<40 mmol/liter)
- Obstructive azoospermia
Cystic Fibrosis – Overview

- **Definition** - AR disease (neonatal-adulthood onset) multisystem disease of epithelial ion transport caused by mutations in the CF transmembrane conductance regulator gene (CFTR)
- **Incidence** – 1 in 1600-3200 US whites affected with CF (1 in 20 carrier rate)
- **Pathogenesis** – (gene for CFTR is on 7p) CFTR is a cAMP regulated Cl-channel that regulates other ion channels; CFTR maintains hydration of secretions of airways and ducts through the transport of chloride and inhibition of Na uptake; CFTR dysfunction affects many organs that secrete mucous (respiratory/GI tract, pancreas, biliary system, male genitalia, sweat glands)
- **Diagnosis** – 1+ phenotypic features (pulmonary, meconium ileus, growth failure, obstructive azospermia, exocrine pancreatic insufficiency) + 2 CFTR mutations or abnormal sweat chloride (>60 MEQ/L)
Hyperaerated lungs, pulmonary blebs
http://www.eradimaging.com/im
Cystic fibrosis – genetic principles

- Ethnic variation - CFTR mutation detection rate varies by test method and ethnic background; in some affected and carrier individuals the disease-causing mutation is not detectable

- Genetic modifiers -
  - correlation between particular CFTR mutant alleles and disease severity (pancreatic insufficiency) or spectrum of disease associated with a particular disease causing mutation that alters protein production
  - some mutations in CFTR cause disease manifestations only in certain tissues (e.g. some mutations affecting the efficiency of splicing have a greater effect on Wolffian duct derivatives than in other tissues because of a tissue-specific need for full-length transcript and protein)

- Environmental modifiers - cigarette smoke worsens severity of lung disease
## Cystic Fibrosis

### Table 1. Cystic Fibrosis Detection and Carrier Rates Before and After Testing

<table>
<thead>
<tr>
<th>Racial or Ethnic Group</th>
<th>Detection Rate</th>
<th>Carrier Rate Before Testing</th>
<th>Carrier Risk After Negative Test Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashkenazi Jewish</td>
<td>94%</td>
<td>1/24</td>
<td>Approximately 1/400</td>
</tr>
<tr>
<td>Non-Hispanic Caucasian</td>
<td>88%</td>
<td>1/25</td>
<td>Approximately 1/208</td>
</tr>
<tr>
<td>Hispanic American</td>
<td>72%</td>
<td>1/46</td>
<td>Approximately 1/164</td>
</tr>
<tr>
<td>African American</td>
<td>65%</td>
<td>1/65</td>
<td>Approximately 1/186</td>
</tr>
<tr>
<td>Asian American</td>
<td>49%</td>
<td>1/94</td>
<td>Approximately 1/184</td>
</tr>
</tbody>
</table>

ACOG committee opinion 2006
Cystic fibrosis & Pregnancy

• Inheritance, recurrence risk – autosomal recessive inheritance implications, depends on ethnic background

• ‘Prenatal diagnosis is based on identification of the CFTR mutations in DNA from fetal tissue...effective identification of affected fetuses usually requires that the mutations responsible for CF in a family have already been identified.’ (Nussbaum case review)

• Predictors of poor pregnancy outcome – FEV-1 <40-50% (OMIM, Moskowitz), pregnancy hastens progression to death; FEV >70% - pregnancy tolerated well

• Management – accurate/confirmed diagnosis, symptomatic management (bronchodilators – continue), control of infection, pancreatic enzymes (oral, continue), nutrition, lung transplant, tobramycin
CF – CI to pregnancy

- Cor pulmonale (echocardiogram recommended to clear patient prior to pregnancy)
  - RV dilation
  - RV failure
  - Pulmonary HTN
Case 3

• 30 yo P0000
• History of cystic fibrosis
• 12 weeks
• Evaluation/management?
• Should screen for cor pulmonale
TB
Tuberculosis

- Bacterium – Mycobacterium tuberculosis
- Respiratory spread (not by touching, sharing food/drink, touching bed linens or toilet seats, sharing toothbrushes, kissing
- Symptoms of TB disease – severe cough for 3+ weeks, pleuritic chest pain, hemoptysis, weakness/fatigue, weight loss, anorexia, F/C, night sweats
TB - Diagnosis

- Groups to test – exposure to person with TB disease, HIV infection, symptoms of TB disease, from country that TB disease is common (Latin America, the Caribbean, Africa, Asia, Eastern Europe, and Russia), live/work where TB disease is common (homeless shelters, prison or jails, or some nursing homes), illegal drugs

- Testing – Valid and safe in pregnancy (CDC)
- Skin testing - >5mm (CDC) → check CXR
- Interferon-gamma release assay – pt with previous BCG vaccine, unable to do skin test
  - If +, check CXR
TB – Diagnosis/Tx (CDC)

• Latent TB infection (LTBI) - +skin/blood test, negative CXR
  – Incidence to active infection – 3%/year
    • INH 300mg/day x9months, pyridoxine 25mg/d (decrease hepatic toxicity) - CDC
  – HIV + - 8% incidence to active infection

• TB Disease - +skin/blood test, + CXR
  – 4 drug regimen – INH, rifampin, ethambutol, pyrazinamide x9months

• MDR, HIV pt etc – consult CDC website/ID

• Pregnancy – Tx AP to decrease risk of neonatal disease, separation of mother/baby in select cases of active disease
Case 3

- 30 yo P0000
- History of cystic fibrosis
- 12 weeks
- Evaluation/management?
Cystic Fibrosis
EFFECTS OF CYSTIC FIBROSIS
Multisystem disease

- Infection of airways
- Severe hepatobiliary disease (5–10% of cases)
- Pancreatic exocrine insufficiency
- Meconium ileus at birth (15–20% of cases)
- Sweat chloride value usually 90–110 mmol/liter, sometimes 60–90 mmol/liter
- Obstructive azoospermia

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Hyperaerated lungs, pulmonary blebs
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- Genetic modifiers-
  - correlation between particular CFTR mutant alleles and disease severity (pancreatic insufficiency) or spectrum of disease associated with a particular disease causing mutation that alters protein production
  - some mutations in CFTR cause disease manifestations only in certain tissues (e.g. some mutations affecting the efficiency of splicing have a greater effect on Wolffian duct derivatives than in other tissues because of a tissue-specific need for full-length transcript and protein)

- Environmental modifiers - cigarette smoke worsens severity of lung disease
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ACOG committee opinion 2006
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• Inheritance, recurrence risk – autosomal recessive inheritance implications, depends on ethnic background

• ‘Prenatal diagnosis is based on identification of the CFTR mutations in DNA from fetal tissue...effective identification of affected fetuses usually requires that the mutations responsible for CF in a family have already been identified.’ (Nussbaum case review)

• Predictors of poor pregnancy outcome – FEV-1 <40-50% (OMIM, Moskowitz), pregnancy hastens progression to death; FEV >70% - pregnancy tolerated well

• Management – accurate/confirmed diagnosis, symptomatic management (bronchodilators – continue), control of infection, pancreatic enzymes (oral, continue), nutrition, lung transplant, tobramycin
CF – CI to pregnancy

- Cor pulmonale (echocardiogram recommended to clear patient prior to pregnancy)
  - RV dilation
  - RV failure
  - Pulmonary HTN
Case 3

- 30 yo P0000
- History of cystic fibrosis
- 12 weeks
- Evaluation/management?
- Should screen for cor pulmonale
Pulmonary Edema in Preeclampsia

- Occurs in 3% of Women with Preeclampsia
- 70% Occurs Postpartum (Fluid Overload)
- Antepartum Pulmonary Edema Associated with Chronic HTN in 90% Cases
- Risk Factors: Older Women, Multigravidas, Chronic Hypertension
- Associated with Fluid Overload, either Colloid or Crystalloid
Pulmonary Edema in Preeclampsia

• Pathophysiology of Pulmonary Edema
  – Reduced COP
  – Alteration of Capillary Membrane Permeability and Integrity
  – Elevated Pulmonary Vascular Hydrostatic Pressures

• Extravasation of Fluids in Pulmonary Interstitium
Pulmonary Edema in Preeclampsia

- Etiology of Pulmonary Edema
  - Abnormal COP-Wedge Gradient
  - Capillary Leak
  - LV Failure
- Non-hydrostatic Forces can Cause Pulmonary Edema
- Fluid Overload is Common, Presenting with Preeclampsia in Pulmonary Edema is Not (If you see it, think LV failure and know that you are in trouble)
Pulmonary Edema in Preeclampsia

- Risk factors – fluid overload, preeclampsia, tocolysis, uncontrolled hypertension
- Diagnosis of Pulmonary Edema
  - Clinical Diagnosis: Progressive Dyspnea and Chest Discomfort
  - Tachypnea, Tachycardia, Bilateral crackles
  - Confirm with CXR and ABG
  - Don’t Forget about Pulmonary Embolism
Case

- 34 yo P0, admitted for preeclampsia
  - IVF pregnancy
- HD #3, developed progressive dyspnea, crackles on physical exam, oxygen requirements
  - CXR revealed bilateral pleural effusions
- Fluid restriction, diuretics (Lasix 20mgIV), delivery, seizure prophylaxis
CXR of pulmonary edema
Pulmonary Edema in Preeclampsia

• Management
  – Oxygen, Fluid Restriction, Semi-Fowler
  – Accurate intake/output
  – If Fluid Overload, then Lasix, Increasing Doses as Needed
  – Consider PA Catheter: Fluid Overload vs. LV Dysfunction vs. Nonhydrostatic Pulmonary Edema
Indications for PA Catheter in Hypertensive Disease

- Severe preeclampsia with refractory oliguria or pulmonary edema
- Ineffective IV antihypertensive therapy
- Intraoperative or intrapartum cardiac failure
Pulmonary Edema in Preeclampsia – 3 subsets

• Management
  – Intravascular volume depletion (oliguria), low PCWP, high CO, high SVR, low CVP –
    • fluids
  – Renal Vasoconstriction (High PCWP, Normal CO and SVR, uroconcentration):
    • Dopamine – 1-5µg/kg/min; furosemide
  – LV Dysfunction/Failure with Vasospasm (high PCWP, high SVR, low CO <5 L/min) :
    • Needs Afterload Reduction (Sodium nitroprusside 0.25-0.5µg/kg/min IV infusion)
    • Volume Restriction
    • Diuretics (max acute dose of furosemide is 120mg, start with 20-40mg)
  – Mechanical Ventilation for Respiratory Failure (If still Pregnant, Intubate Early rather than Late)
• References provided on request


Cardiac Manifestations of Preeclampsia

- Wedge and CVP Do Not Correlate
- SVR is Low Initially, and then Becomes Very High (along with BP)
- Pulmonary Artery Catheter Findings
  - Elevated SBP, SVR
  - Hyperdynamic LV Function
  - Normal to Increased PCWP
  - Low CVP
  - High Wedge with Low CVP May be Due to Increased Afterload with Volume Depletion
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Conclusions

- FRC decreased by 20%
- PCO2 > 40, respiratory distress, impending failure in pregnant women
- Asthma classes
- Step therapy
- ER if FEV1 <80%, Admit if FEV1 <70%
- Avoid hemabate
End

• ???
References

- Provided on request
- Gabbe Obstetrics Text
- ACOG compendium bulletin – Asthma in Pregnancy
- Foley ICU handbook
Following are notes

• Extra slides
CBAVD (Outflow tract) & Cystic Fibrosis

- Congenital bilateral absence of the vas deferens (CBAVD)
- Diagnosis of *CFTR*-related CBAVD in males established by obstructive azoospermia (due to lack of Wolffian duct structures), low volume of ejaculated semen, absence of vas deferens on clinical or ultrasound examination, and at least one disease-causing mutation in *CFTR*
- Patients with CF - Infertility/obstructive azoospermia - > 95% of male infants with CF have azoospermia due to CBAVD
- Male infertility - CBAVD - accounts for 1-2% of male infertility; ~80% of men with CBAVD have at least 1 mutation in CFTR gene (OMIM, Moskowitz)
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Multisystem disease

- Infection of airways
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Labor and Delivery

• Regional/Lumbar anesthesia
  – reduction of oxygen consumption and minute ventilation during labor
  – can induce bronchospasm

• Meperidine – a/e bronchospasm

• Ketamine can prevent bronchospasm
Means To Provide Noninvasive Oxygen Therapy

- **Nasal cannula**
  - FIO2 24-60%
  - flow rate up to 6 L/min
  - flow rate of ≤4L/min need not be humidified

- **Simple oxygen masks**
  - FIO2 35-50%
  - flow rate 5-10L/min
  - flow rates need to be maintained at 5L/min or higher to avoid rebreathing exhaled Co2 that can be retained in the mask

- **Partial rebreathing mask (simple mask with reservoir bag)**
  - O2 flow should be supplied to maintain the reservoir bag at least 1/3 to ½ full in inspiration
  - flow rate 6-10L/min provides FIO2 40-70% oxygen

- **Nonrebreathing mask (similar to partial rebreather except has a series of one-way valves; one valve is b/n mask and the bag to prevent exhaled air from returning to bag)**
  - delivered FIO2 60-80%
  - min flow rate of 10L/min
Criteria For Diagnosis Of Respiratory Failure (MOVE)

- **Mechanical**
  - vital capacity <15mL/kg
  - max inspiratory force < -25cmH2O
  - respiratory rate >35/min

- **Oxygenation**
  - PaO2 <70mmHg with FIO2 .4
  - P(A-a)O2 >350mmHg with FIO2 1.0

- **Ventilation**
  - PaCO2 >55mmHg (acute) - 40 in preg, worry above 35!
  - dead space /tidal volume (Vd/Vt) >.6

- **End-inspiratory lung inflation inadequate for adequate gas exchange**
Indications For Endotracheal Intubation (GARDD)

- Gastro-pulmonary reflux and aspiration
- Airway obstruction (present or suspected)
- Respiratory arrest (actual or impending)
- Depressed mental status
- Difficulty managing secretions
Indications for Mechanical Ventilation (Invasive or Noninvasive)

- Severe respiratory or combined respiratory and metabolic acidosis
- Sustained respiratory rate of $\geq 40$/minute
- Abnormal breathing pattern suggestive of increased respiratory workload and/or respiratory muscle fatigue
- Depressed mental status
- Severe hypoxemia
Criteria For Determining Readiness For Extubation

- PaO₂ > 80 mmHg on FIO₂ 0.6
- PaCO₂ < 45 mmHg
- RR < 35 breaths/min
- TV > 5 mL/kg
- VC > 10 mL/kg
- minute ventilation < 10 L/min
- negative inspiratory force < -20 cmH₂O
- shallow breathing index (resp frequency/tidal vol < 80)
Respiratory physiology in pregnancy

• Upper airways
  – Mucosal edema
  – Capillary engorgement
  – Edema in preeclamptics, patients that have been aggressively hydrated

• Chest wall
  – increase in chest wall circumference (6cm)
  – elevation of diaphragm (5cm)
  – widening of costal angles (from 70 to 104 degrees)
  – increase in diaphragmatic excursion (1.5cm)
  – all of these changes occur before increases of uterine size, maternal body weight, or intraabdominal pressure
Table 1. Classification of Asthma Severity and Control in Pregnant Patients

<table>
<thead>
<tr>
<th>Asthma Severity* (Control†)</th>
<th>Symptom Frequency</th>
<th>Nighttime Awakening</th>
<th>Interference With Normal Activity</th>
<th>FEV₁ or Peak Flow (Predicted Percentage of Personal Best)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermittent (well controlled)</td>
<td>2 days per week or less</td>
<td>Twice per month or less</td>
<td>None</td>
<td>More than 80%</td>
</tr>
<tr>
<td>Mild persistent (not well controlled)</td>
<td>More than 2 days per week, but not daily</td>
<td>More than twice per month</td>
<td>Minor limitation</td>
<td>More than 80%</td>
</tr>
<tr>
<td>Moderate persistent (not well controlled)</td>
<td>Daily symptoms</td>
<td>More than once per week</td>
<td>Some limitation</td>
<td>60–80%</td>
</tr>
<tr>
<td>Severe persistent (very poorly controlled)</td>
<td>Throughout the day</td>
<td>Four times per week or more</td>
<td>Extremely limited</td>
<td>Less than 60%</td>
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Abbreviation: FEV₁, forced expiratory volume in the first second of expiration
*Assess severity for patients who are not taking long-term-control medications.
†Assess control in patients taking long-term-control medications to determine whether step-up therapy, step-down therapy, or no change in therapy is indicated.

Table 2. Comparative Daily Doses for Inhaled Corticosteroids*

<table>
<thead>
<tr>
<th>Corticosteroid</th>
<th>Amount</th>
<th>Low Dose</th>
<th>Medium Dose</th>
<th>High Dose</th>
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<tbody>
<tr>
<td>Beclomethasone HFA</td>
<td>40 mcg per puff</td>
<td>2–6 puffs</td>
<td>More than 6–12 puffs</td>
<td>More than 12 puffs</td>
</tr>
<tr>
<td>80 mcg per puff</td>
<td>1–3 puffs</td>
<td>More than 3–6 puffs</td>
<td>More than 6 puffs</td>
<td></td>
</tr>
<tr>
<td>Budesonide</td>
<td>200 mcg per inhalation</td>
<td>1–3 puffs</td>
<td>More than 3–6 puffs</td>
<td>More than 6 puffs</td>
</tr>
<tr>
<td>Fluticasone</td>
<td>250 mcg per puff</td>
<td>2–4 puffs</td>
<td>4–8 puffs</td>
<td>More than 8 puffs</td>
</tr>
<tr>
<td>Fluticasone HFA</td>
<td>44 mcg per puff</td>
<td>2–6 puffs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>110 mcg per puff</td>
<td>2 puffs</td>
<td>2–4 puffs</td>
<td>More than 4 puffs</td>
<td></td>
</tr>
<tr>
<td>220 mcg per puff</td>
<td>1–2 puffs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluticasone DPI</td>
<td>50 mcg per inhalation</td>
<td>2–6 puffs</td>
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<tr>
<td>100 mcg per inhalation</td>
<td>1–3 puffs</td>
<td>3–5 puffs</td>
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<tr>
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<td>1 puff</td>
<td>2 puffs</td>
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<tr>
<td>Mometasone</td>
<td>200 mcg per inhalation</td>
<td>1 puff</td>
<td>2 puffs</td>
<td>More than 2 puffs</td>
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<tr>
<td>Triamcinolone</td>
<td>75 mcg per puff</td>
<td>4–10 puffs</td>
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*Total daily puffs is usually divided into a twice-per-day regimen.
Abbreviations: DPI, dry powder inhaler; HFA, hydrofluoroalkane
ARDS – diagnostic criteria

• I - acute onset
• II - history compatible with certain risk factors
  – trauma
  – severe shock
  – sepsis (septic Ab included)
  – aspiration
  – venous fluid, fat or amniotic fluid embolism
  – pneumonia
  – pancreatitis
  – blood transfusion
  – seizures
  – overdose
  – drug induced
  – eclampsia
  – abruptio placentae
  – dead fetus syndrome or retained POC
  – DKA
• III – clinical exclusion of cardiogenic pulmonary edema (or PCWP < 18mmHg
• IV – respiratory distress
• V – diffuse bilateral patchy opacities in CXR
• VI- PaO2/FIO2 of <200 (less severe form with this between 201-300mmHg
ARDS – principles of treatment

• Therapeutic goals
  – adequate oxygenation
  – avoid barotrauma with treatment
  – avoid cardiovascular compromise

• Management
  – semi-fowler position – elevate head and chest to improve ventilation
  – oxygen – 10L/min with nonrebreather face mask or CPAP; consider intubation
  – continuous pulse oxymetry and cardiac monitoring
  – IV access; consider arterial line or central line
  – ID risk factors, modify if possible
ARDS – principles of treatment

• Pharmacologic therapy
  – no specific tx
  – NO, pulmonary vasodilators, surfactant, prone ventilation, ECMO
Pulmonary edema

- **Diagnosis**
  - progressive not sudden dyspnea
  - desaturation
  - tachypnea
  - ? HTN
  - bilateral crackles
  - S3/Gallop (not always)

- **RF**
  - fluid overload
  - preeclampsia
  - tocolytic treatment
  - uncontrolled hypertension
Pulmonary edema

• **Management**
  - semi-fowler position – elevate head and chest to improve ventilation
  - oxygen – 10L/min with nonrebreather face mask or CPAP; consider intubation
  - continuous pulse oxymetry and cardiac monitoring
  - IV access; consider arterial line or central line
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• **Monitoring**
  - input/output
  - BP, fetal heart rate
Pulmonary edema

• Pharmacologic therapy
  – Morphine sulfate – 3-5mg IV (avoid if altered LOC, increased ICP or severe COPD)
  – Furosemide 20-40 mg IV, repeat prn, do not use >120mg/hr and give slowly to prevent ototoxicity
  – Nitroglycerin (2 in of paste or 1 pill 1/150 until IV access obtained)
  – Hydralazine 5-10mg IV if severe HTN is causing the pulmonary edema
Case 1

- 28yo P0
- 12 weeks
- Hx of asthma-
- Takes rescue inhaler daily
- No maintenance medication
- Management?
Case 2

• 30 yo P4004 at 20 weeks’ gestation, healthy, presents to ED for altered mental status, somnolent, HA, dizziness, palpitations, n/v. Husband reports pt was sleeping in back room of house with space heaters.

• Diagnosis/Treatment?