

Asthma & Pregnancy

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Asthma & Pregnancy

Disclosure of Conflict of Interest Information

I have the following relationships that exist related to this presentation:

The following companies have contracted with the University of Chicago with me as principal investigator to conduct research studies: GlaxoSmithKline and AstraZeneca.

“The care of the woman with asthma when she is pregnant differs little from that when she is not.”

Greenburger & Patterson, *NEJM* 312:897, 1985

Case #1: Prenatal Counseling

- 34-year old woman with **moderate persistent** asthma
- Followed in pulmonary clinic for years with well-controlled asthma on inhaled fluticasone and salmeterol
- Now presents requesting **medication adjustment** prior to conception

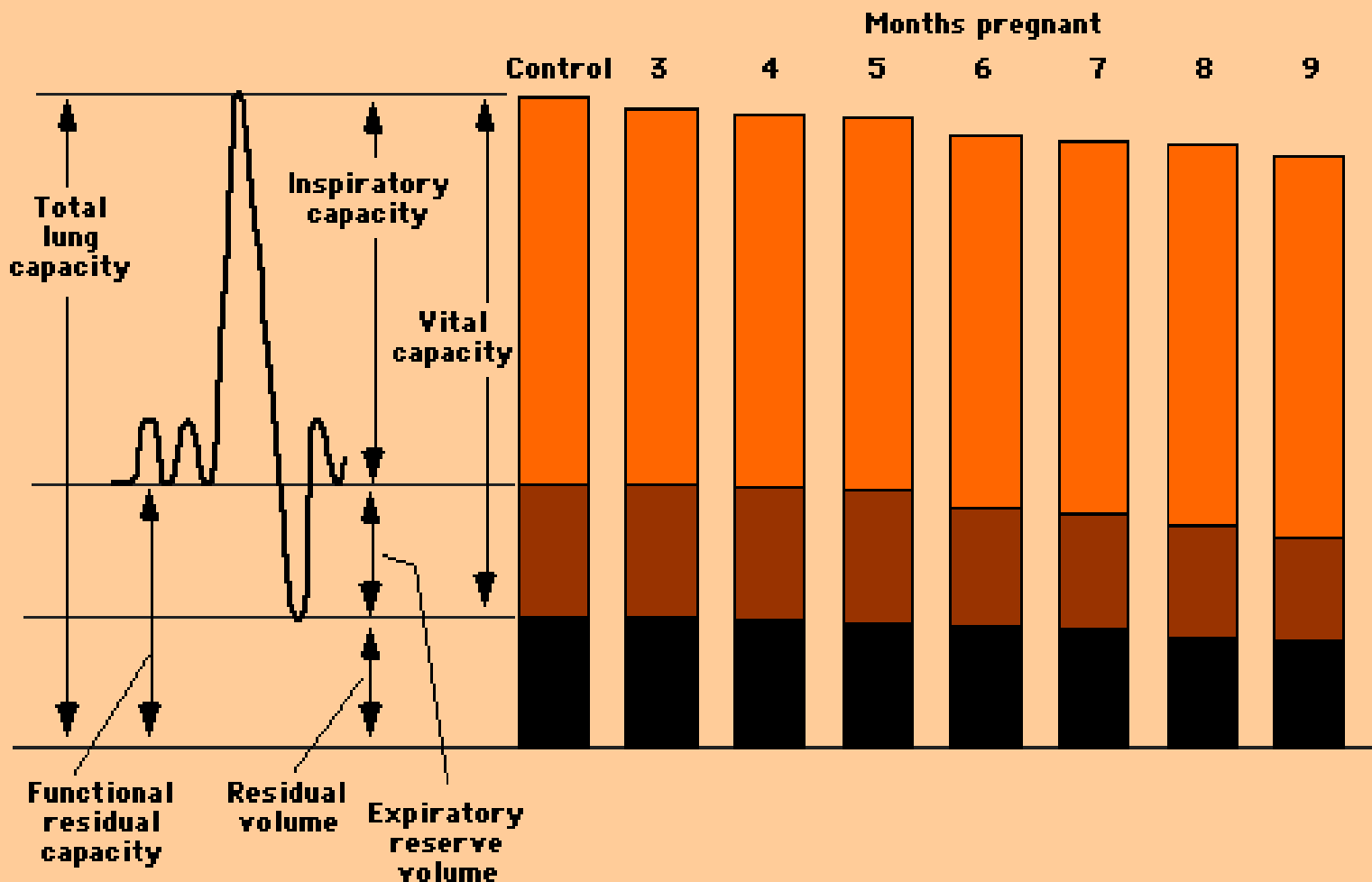
Case #2: Acute Asthma Exacerbation

- 43-year old woman with **severe persistent** asthma
- Presents to pulmonary clinic after **2 hospitalizations** for asthma during first trimester of pregnancy
- No further hospitalizations but required multiple asthma medications and frequent clinic visits
- Presents to the **emergency room** at 32 weeks gestation with an acute severe asthma attack

Asthma & Pregnancy

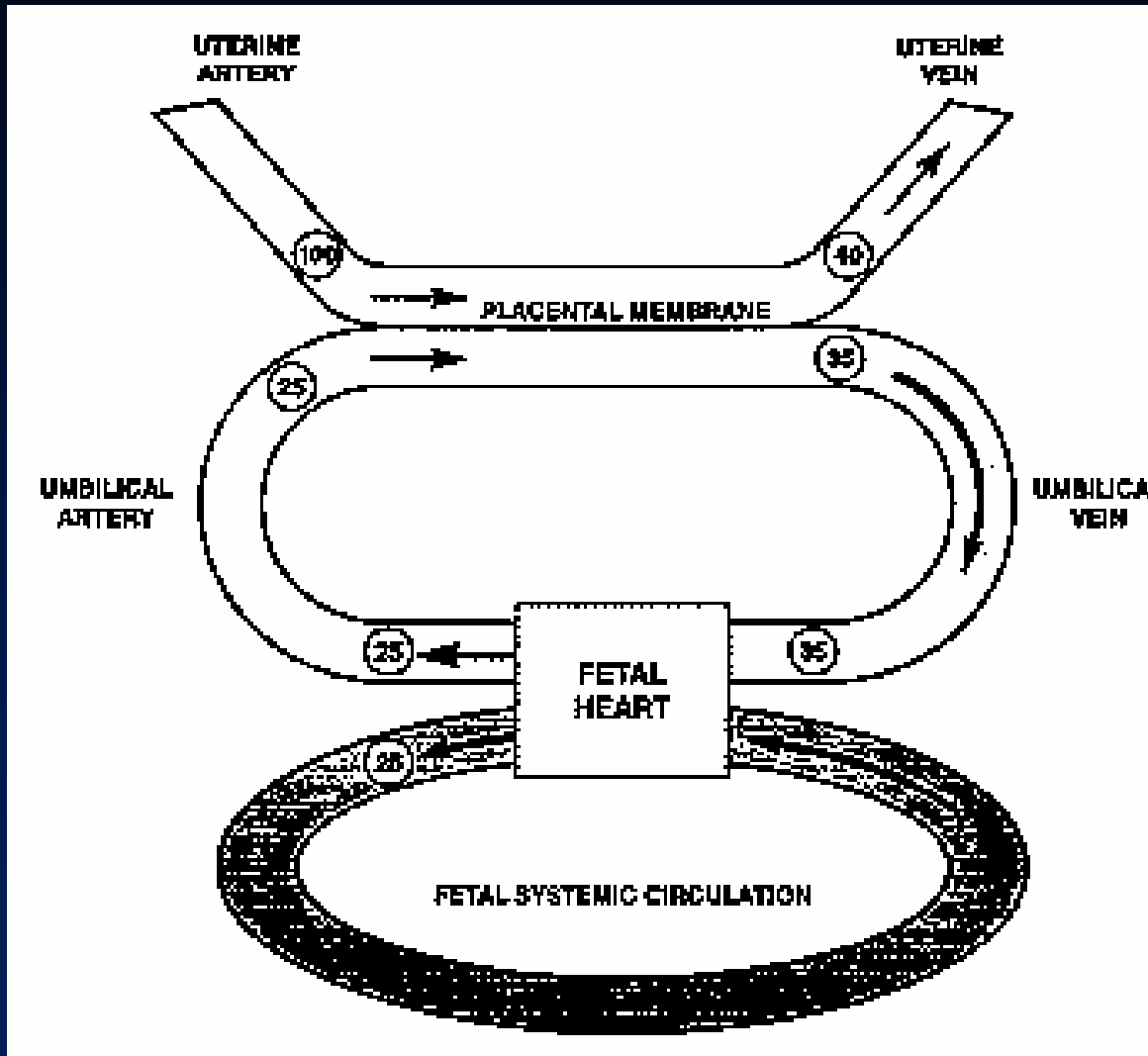
- **General Considerations**
- **Medication Safety**
- **Management**
- **Cases**

Pulmonary Function Tests in Pregnancy



- Decreased chest wall compliance
- **FRC ↓ 20%** from ↓ in both ERV and RV
- TLC not much changed due to ↑ IC
- **No change** FVC, flows, NIF, PEF

Maternal-Fetal Oxygen Transfer



- O₂ delivery depends on uterine artery blood flow /maternal O₂ content
- Maternal and fetal blood run in same direction (**concurrent exchange mechanism**)
- Umbilical vein blood then mixes with deoxygenated blood in fetal IVC
- Fetal environment relatively hypoxic with **low umbilical vein pO₂**

Lupinsky, *AJRCCM* 152:427, 1995

Effect of Pregnancy on Asthma

Rule of Thirds

- In 1/3 of patients asthma unchanged
- In 1/3 of patients asthma improves (23%)
- In 1/3 of patients asthma deteriorates (30%)

Effect of pregnancy on asthma tends to be similar in successive pregnancies

Severe asthma predisposes to worsened control

Effect of Pregnancy on Asthma

Category

Characteristic

Improvement

Progressive improvement throughout pregnancy

Maximum improvement in last 4 weeks of pregnancy

Deterioration

Exacerbations peak between 24 and 36 weeks of gestation

URI and poor control most common precipitants

May improve in the last 4 weeks of pregnancy

Schatz, J Allergy Clin Immunol 81:509, 1988

Labor, Delivery and Postpartum

- 90% of women with asthma have no symptoms during labor or delivery
- **Rarely require** treatment beyond bronchodilators
- Improved airway function in last 4 weeks of pregnancy may help prevent asthma symptoms during L&D
- Patients return to their original asthma status by 3 months postpartum

Potential Risks from Maternal Asthma

Maternal health risks

↑ maternal mortality

gestational hypertension

C-section

hyperemesis

preeclampsia

vaginal hemorrhage

placenta previa

Fetal health risks

↑ perinatal mortality

low birth weight

small for gestational age

↑ neonatal hypoxia

preterm birth

congenital anomalies

Risks from Maternal Asthma

- Historical **cohort analysis** births NJ **1989-1992**
- 2,289 women with asthma (ICD-9) vs 9,156 controls
- Asthma patients were younger, less educated, single, AA or Hispanic, less prenatal care, smokers, increased rates of DM and HTN
- Infant outcomes: ↑ preterm delivery, low birth weight, small for gestational age, congenital anomalies, prolonged hospital stay
- Maternal outcomes: preterm labor, placenta previa, **pre-eclampsia**, C-section, **prolonged hospital stay**

Demissie, *AJRCCM* 158:1091,1998

Outcomes in Aggressive Management of Asthma in Pregnancy

- **Inception cohort** trial of 972 pregnant women in an HMO
- Half had **documented asthma** by ATS criteria
- Subjects matched for age, parity, year of delivery, smoking
- Asthma managed by **step therapy** to prevent symptoms that interfered with sleep and daily activity
- Perinatal, fetal, maternal outcome variable measured

Schatz, *AJRCCM* 151:1170, 1995

Outcomes in Aggressive Management of Asthma in Pregnancy

- Adequate asthma control in all cases
- Asthmatic pregnant women on oral corticosteroids had a higher incidence of hypertension (3.7 vs 1.0%)
- Perinatal outcomes **similar** in both groups
- Maternal complications **similar** in both groups
- Infant outcomes **similar** in both groups

Schatz, *AJRCCM* 151:1170, 1995

Asthma & Pregnancy

Medication Safety

NAEPP Update 2004 05-5236, 2005

www.nhlbi.nih.gov/health/prof/lung/asthma/astpreg.htm

Current Options for Treating Asthma

- **Long-Term Controllers**

- Corticosteroids (inhaled and systemic)
- Long-acting beta₂-agonists
- Leukotriene modifiers
- Theophylline
- Cromolyn

- **Quick relief**

- Short-acting inhaled beta₂-agonists

FDA Pregnancy Risk Classification for Drugs

- Category A** No risk demonstrated in 1st trimester in controlled studies in women, no risk in later trimesters
- Category B** No risk in animal studies, but controlled studies in women not done
- Category C** Fetal harm in animals, no studies in women (or studies in animals & women not available)
- Category D** Evidence of human fetal risk, but benefits > risk in life-threatening situations
- Category X** Contraindicated in pregnant women

Potential Adverse Effects of Common Asthma Drugs on the Fetus

Corticosteroids	preeclampsia, preterm and low birth weight, cleft palate 1st TM (incidence 0.3%)
Theophylline	↑ HR, vomiting, jitteriness (moms/fetus) ↑ when maternal levels > 12 mcg/mL
Systemic β_2 Agonists	↑ fetal HR, ↑ neonatal HR, tremor, hypoglycemia
LT modifiers	not known, animal data teratogenicity zileuton
Decongestants	Uterine vasoconstriction, fetal gastroschisis

Safety of Beta-agonists in Pregnancy

- Six human studies support **safety of short-acting beta₂-agonists** in pregnancy (1,599 pregnant woman)
- Limited data on **long-acting beta₂-agonists** but similar pharmacologic and toxicologic profiles to short-acting drugs suggest they are **okay for use**
- Occasional episodic use epinephrine for severe, acute asthma attack is okay

Safety of Inhaled Steroids in Pregnancy

- Swedish Medical Birth Registry 1995-97
- 2,014 infants with mothers who had used **budesonide** in early pregnancy
- 75 infants (3.8%) had congenital malformation vs 3.5% in general population
- 4 infants with cleft palate vs 3.3 expected
- **No teratogenic** effect of budesonide

Kallen, *Obstet Gynecol* 93:392,1999

Asthma Medications Presumed Safe in Pregnancy

- **Beta₂-agonists** both short/long-acting (**category C**)
- **Inhaled corticosteroids (category C)**, especially beclomethasone and **budesonide**
- Theophylline (category C)- Clearance ↓ 3rd trimester
- Oral corticosteroids, if indicated (category C)
- Cromolyn sodium (category B)
- Loratadine and cetirizine

Medications to be Discouraged in Pregnancy

- **Frequent injections epinephrine (category C)**
- **Oral decongestants in the first trimester**
- **Iodine-containing cough medications**
- **Tetracycline (category D)**
- **Aspirin and NSAID (category D)**
- **Beta-blockers**
- **Prostaglandins**

Asthma & Pregnancy

Management

Goals of Asthma Treatment during Pregnancy

- Control symptoms, including nocturnal symptoms
- Prevent acute exacerbations
- No limitations on activities
- Maintain (near) **normal pulmonary function**
- Minimal use short-acting inhaled beta₂-agonists
- **Protect the mother and fetus from adverse effects**

General Principles

- **Preconception**
 - Optimize asthma management
 - **Few changes in treatment regimen** are needed in pregnancy especially if asthma is controlled
- **Avoid recently introduced medications whose safety in pregnancy is not established**
- **Use adequate doses of medications to control symptoms and avoid hypoxia**
- It is **essential** to maintain adequate oxygenation to the fetus

Components of Asthma Management

- Objective measures for assessment and monitoring
- Patient education
- Avoidance of factors contributing to asthma severity
- Pharmacologic therapy- **follow NIH stepwise guidelines to therapy**
- Diagnose and treat **rhinitis, sinusitis or gastroesophageal reflux disease** if present

Optimizing Non-Pharmacological Measures

- Education and PEF monitoring
- Avoid asthma triggers
- **Stop smoking**
- Minimize URI with saline washes
- Postural drainage for mucus plugs
- Relaxation techniques for mild symptoms

Environmental Control in Asthma

eliminate these “mobile allergen bearing units”



Step 1 – Mild Intermittent Asthma

Clinical Presentation

Intermittent symptoms

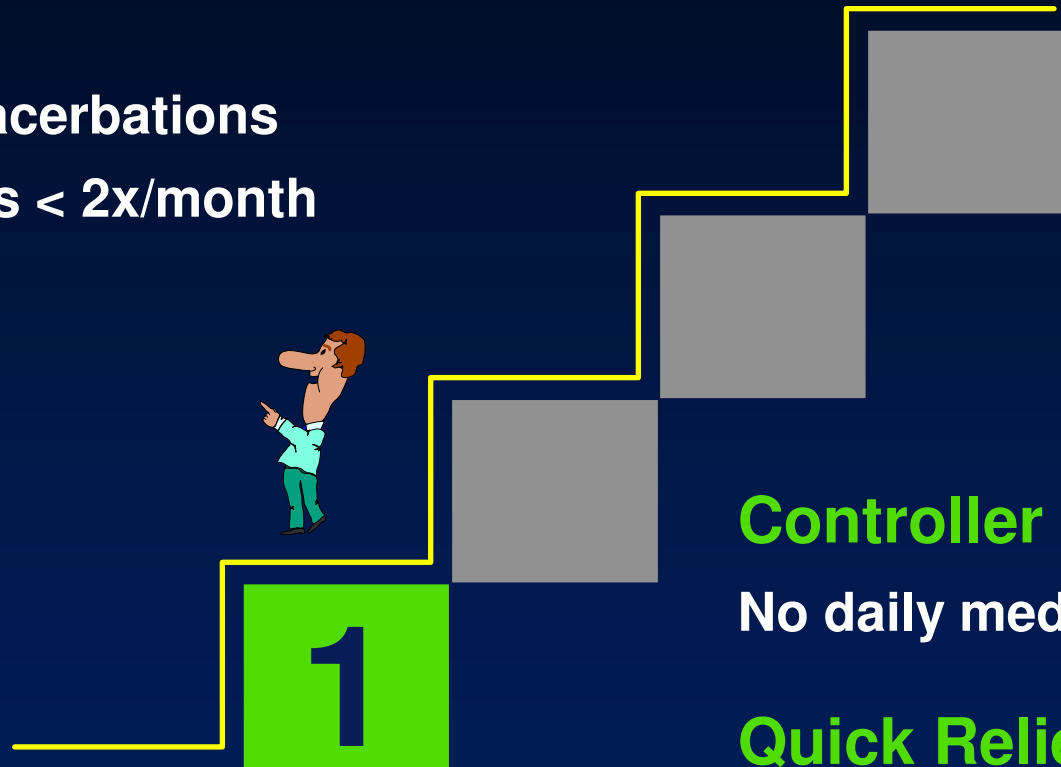
Brief exacerbations

Normal between exacerbations

Nighttime symptoms < 2x/month

PEF or FEV₁ is:

> 80% predicted



Controller

No daily medication needed

Quick Relief

Inhaled β_2 -agonist prn

(Albuterol)

Step 2 – Mild Persistent Asthma

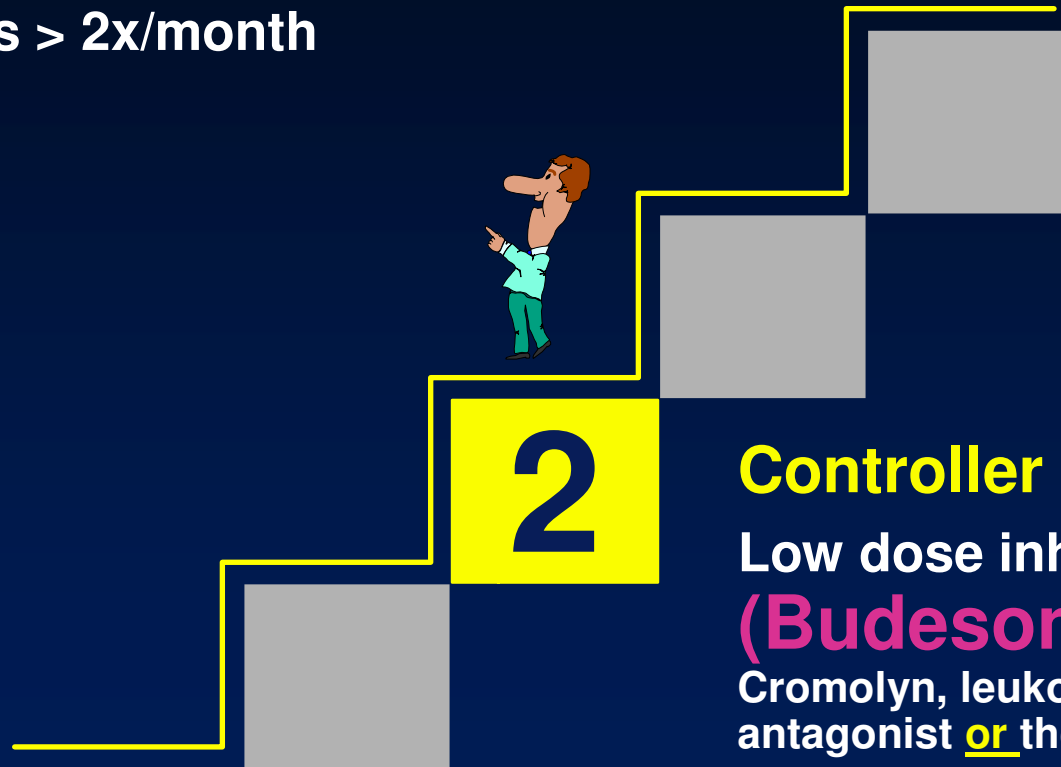
Clinical Presentation

Symptoms > 2x/wk

Nighttime symptoms > 2x/month

PEF or FEV₁ is:

> 80% predicted



Controller

Low dose inhaled steroid
(**Budesonide**)
Cromolyn, leukotriene receptor
antagonist or theophylline

Quick Relief

Inhaled β_2 -agonist prn
(**Albuterol**)

Step 3 – Moderate Persistent Asthma

Clinical Presentation

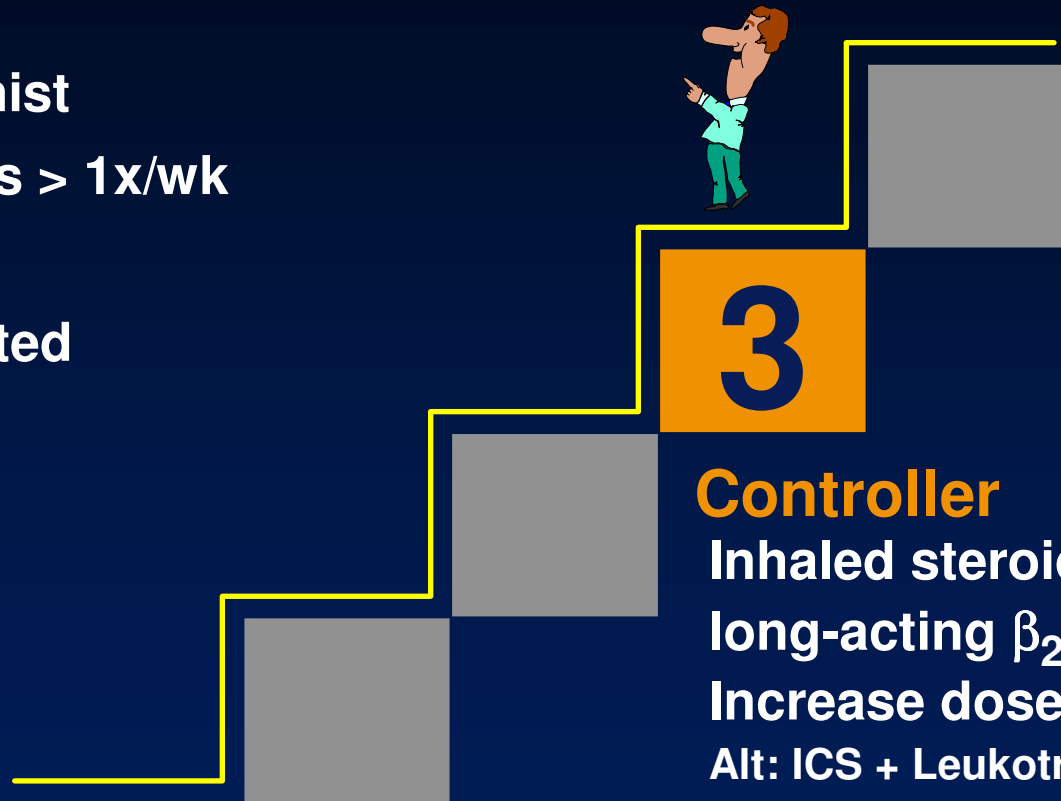
Daily symptoms

Daily use of β_2 -agonist

Nighttime symptoms > 1x/wk

PEF or FEV₁ is:

60 – 80% predicted



Controller

Inhaled steroid +
long-acting β_2 -agonist or
Increase dose inhaled steroid

Alt: ICS + Leukotriene receptor antagonist
or theophylline

Quick Relief

Inhaled β_2 -agonist prn

Treatment – Severe Persistent Asthma

Clinical Presentation

Daily symptoms

Frequent nocturnal awakenings

Frequent exacerbations

PEF or FEV₁ is:
≤ 60% predicted



4

Controller

Inhaled steroid (high-dose)

Long acting β_2 -agonist and if needed

Oral steroids

Quick Reliever

Short acting inhaled β_2 -agonists

Management of Acute Asthma in Pregnancy

- Prospective case cohort study of **acute asthma** patients presenting to ER in 18 states
- Pregnant vs nonpregnant matched for severity of illness (by PEFR, duration of symptoms, admission rate)
- For patients D/C from ER, significantly **less use of CS** and greater likelihood for continued exacerbation at two weeks in pregnant cohort

Asthma in Pregnancy- Benefit ICS

- Stenius-Aarnial et al; Thorax 1996; 51:411
 - Observational study
 - Comparing **ICS use or not** in pregnant asthmatics, incidence of acute asthma was **18% vs 4%** ($p < 0.0001$)
- Wendel et al; AJOG 1996; 175:150
 - Prospective randomized controlled study of acute asthma
 - Beta-agonist and steroid taper vs beta-agonist/steroid taper + **ICS** at time of discharge from hospital
 - Readmission rate **33% vs 12%** ($p < .05$)

Case #1: Initial Presentation

- 34-year old woman with moderate asthma wants to **adjust asthma medications** prior to planned pregnancy.
- History: Lifelong nonsmoker. Mild asthma since childhood. Lives with a smoker and a cat. **First pregnancy 2 years ago** with **very mild** initial increase in symptoms during that pregnancy. Now well.
- Meds: Albuterol MDI 2 puffs prn, salmeterol (Serevent) MDI 2 puffs BID, fluticasone (Flovent) 2 puffs BID, theophylline (Theodur) 300/200 mg QD, budesonide (Rhinocort) nasal spray.
- Exam: Thin woman in no acute distress. Lungs: clear.
- Spirometry: FEV₁ 3.21L (88% predicted)

Case #1: Treatment

- Avoid cats and cigarette smoke
- Monitor PEFr
- Continue fluticasone (or change to budesonide) and salmeterol
- Continue albuterol and nasal budesonide
- Continue theophylline but carefully monitor blood levels especially 3rd trimester

Case #2: Initial Presentation

- 43-year old woman with asthma and sinus disease who is 13 weeks pregnant with first child.
- CC: **Management asthma.**
- History: Current **cigarette smoker** (1/2 ppd). Diagnosed with asthma in high school. Never hospitalized or intubated. Required oral corticosteroids in past to control asthma. Since pregnancy has had marked increase in symptoms including wheezing, chest tightness, cough and sputum. **Two hospitalizations** in 1st trimester. Has required prednisone to control symptoms. Also notes chronic sinus disease. Better but still has mild wheezing.

Case #2: Initial Presentation

- **PMH: Depression**
- **Meds: Albuterol MDI 2 puffs prn, flunisolide (Aerobid) 4 puffs BID, prednisone 50 mg QD, beclomethasone nasal spray, sertraline (Zoloft) 50 mg QD.**
- **Exam: Obese woman in no acute distress. HEENT: No nasal polyps. Lungs: mild expiratory wheezing. Cor: Normal S1, S2. Abdomen: Striae. Ext: No c/c. Mild pedal edema.**
- **Spirometry: FEV₁ 1.91L (73% predicted)**

Case #2: Treatment

- **STOP SMOKING**
- **Monitor spirometry in clinic and PEFr at home**
- **Continue albuterol and beclomethasone nasal spray**
- **Change to inhaled fluticasone and salmeterol (Advair)**
- **Slowly taper prednisone**

Case #2: Course

- She was seen frequently in clinic with persistent symptoms and ↓ flows requiring the addition of theophylline and continued oral prednisone. She developed hyperemesis and the theophylline had to be discontinued. **At 31 weeks** she developed **↑ wheezing**, cough and sputum production.
- Meds: Albuterol MDI 2 puffs prn, Advair 500/50 2 puffs BID, prednisone 20 mg QD, budesonide nasal spray, sertraline (Zoloft) 50 mg QD.
- Exam: Obese woman in mild distress. Lungs: mild expiratory wheezing. Cor: Normal S1, S2.
- Spirometry: FEV₁ 1.44L (55% predicted)

“A decision to avoid use of effective pharmacologic agents in a symptomatic pregnant asthmatic is a willful act of neglect.”

Barron & Leff, *ARRD* 147:510, 1993

Summary- Asthma in Pregnancy

- Most **frequent** respiratory disorder of pregnancy
- Clinical course follows “**Rule of thirds**” with more severe asthma more likely to worsen
- **Pharmacologic management differs little** from that of nonpregnant woman
- Both inhaled bronchodilators and ICS safe in pregnancy
- Maternal and fetal outcomes are improved by **aggressively controlling asthma**