Effect of Pregnancy and Hormonal Changes on Asthma

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Disclosure

Nothing to disclose

Learning Objectives

At the conclusion of this session, the participant should be able to:

• Describe recent studies on the effects of menarche and menopause on asthma
• Describe recent studies on the effects of pregnancy on asthma
• Discuss implications of these recent findings for patients with asthma
Overview of Presentation

1. Gender/sex-related influences
2. Female sex hormones
3. Menarche → asthma
4. Menopause → asthma
5. Pregnancy → asthma
6. Summary

Gender/Sex-related Influences

• Complex mixture of influences on asthma:
  – Social and environmental factors (gender-related)
  – Genetic and hormonal factors (sex-related)

• Female vs. male differences in asthma prevalence by age:
  – Children: male >> female
  – Adolescents and adults: female >> male
  – Older adults: female > male

F:M Ratio – Asthma Prevalence by Age

Schatz & Camargo, Ann Allergy Asthma Immunol 2003
Prevalence of Current Asthma by Age

Differences in Asthma-related Events

Compared with men, women have:

• Higher symptom frequency, symptom intensity, and resulting activity limitations
• More ED visits
• More hospitalizations, with longer LOS
• More asthma deaths

Potential Explanations

• Social factors (including diagnostic bias)
• Environmental factors
  – Obesity
  – Sedentary lifestyle
  – Smoking
• Genetics
• Sex hormones
Female Sex Hormones

- Estrogen
  - Both immunostimulatory & immunosuppressive
  - Estrogen receptor-α deficient mice have ↑ AHR
  - In humans, unclear association between estrogen levels and AHR or asthma severity/control
- Progesterone
  - Possible relaxation of bronchial smooth muscle
  - In humans, unclear association with progesterone levels and AHR or asthma severity/control

Menarche → Asthma

Traditional highlights:
- ↑ risk of incident asthma after menarche
- Premenstrual asthma common
  - 1/3 of asthmatic women
  - Subset with more severe asthma
  - Peak symptoms 2-3 days before menses

ED Visits By Day of Menstrual Cycle

Zimmerman, AJRCCM 2000
**ED Visits By Day of Menstrual Cycle**

![Graph showing ED visits by day of menstrual cycle]

**BHR Over Menstrual Cycle**

- Swiss cohort study on Air Pollution And Lung Disease in Adults (SAPALDIA)
- 571 menstruating women without hormonal treatment, ages 28-58 years
- Perimenstrual: 3 days before and after first day of menstruation; n=143
- Methacholine challenge; BHR 13%
- Role of oral contraceptive (OC) as effect-modifier; same sample + 130 taking OCs

Dratva, JACI 2010

**Cyclic Pattern of BHR**

![Graph showing cyclic pattern of BHR]

Dratva, JACI 2010
Age of Menarche, Lung Function, Asthma

- European Community Respiratory Health Survey II
- 3,354 women, age 27-57 years
- Age of menarche; age ≤10y 3.4%
- Outcomes
  - Spirometry
  - Asthma symptoms
  - Asthma with BHR
  - Asthma symptom score

Macsali, AJRCCM 2011

FEV₁ and FVC by Age of Menarche

Macsali, AJRCCM 2011

Asthma Outcomes by Age of Menarche

Macsali, AJRCCM 2011
Age of Menarche and Risk of Asthma

- National Longitudinal Survey of Children & Youth (Canada): age 8-11 y → 18-21 y
- 1,176 girls (weighted n=352,345)
- Early menarche = age <11.56 y (1 SD less than average age of 12.66 y); ~14%
- Report of doctor-diagnosed asthma
- Girls with early menarche had >2x risk of incident asthma during early adulthood (adjusted OR 2.34, 95%CI 1.19-4.59)

Al-Sahab, Am J Epidemiol 2011

Menopause → Asthma

Traditional highlights
- ↓ asthma prevalence in older women lowers the F:M ratio
- Hormone replacement therapy (HRT) ↑ risk of incident asthma
- Menopausal asthma
  - Subset with more severe asthma
  - Absence of atopy; no family history of asthma

Barr, Arch Intern Med 2004

Incident Asthma or COPD by HRT
Menopause, Lung Function, Symptoms

- European Community Respiratory Health Survey II, 2002
- 1,274 women, age 45-56 years, not on HRT
- Menopausal transition = amenorrhea for last 6 months (n=432; 34%)
- Outcomes:
  - Spirometry
  - Respiratory symptoms
- Role of BMI as effect-modifier

Gomez Real, JACI 2008

Amenorrhea and Respiratory Symptoms

Gomez Real, JACI 2008

Amenorrhea and FEV<sub>1</sub>

Gomez Real, JACI 2008
Interaction with BMI?

Menopausal Asthma: New Phenotype?

- Three groups of Italian women:
  - 40 with menopausal asthma
  - 35 with premenopausal asthma
  - 30 age-matched healthy controls
- Outcomes:
  - Urinary LTE4
  - Induced sputum inflammatory cells
  - Exhaled LTE4, IL-6, pH, NO
- Menopausal: ↑ sputum neutrophils, ↑ exhaled IL-6
- Premenopausal: ↑ sputum eosinophils

Pregnancy → Asthma

Traditional highlights:
- Multiple physiologic changes beyond hormones
- Asthma improves for 1/3, same for 1/3, worse for 1/3*
- Mechanism(s) unclear
- Later pregnancies tend to have similar asthma course

NAEPP Working Group Reports:
- 1993
- Update 2004
- Optimal care improves maternal & fetal outcomes

* Kircher, Ann Allergy Asthma Immunol 2002
Pregnancy → Asthma  
(continued)

• Effect of pregnancy on asthma
  – No major advances in past 2-3 years
  – eg, relevance of 1/3 rule today is unclear
  – eg, mechanisms for 1/3 rule remain unclear

• Effect of asthma on pregnancy (and children)
  – Multiple recent studies support importance of asthma control
    for both pregnant mother and child
  – Likewise, multiple studies support overall safety of EPR3
    recommendations for pregnant women (benefit >> risk)

• Improve asthma control during pregnancy

FENO Measurement During Pregnancy

• Double-blind, parallel-group RCT
• 220 pregnant, non-smoking, Australian women
• Randomly assigned by 22 weeks gestation to
  ICS adjustment at monthly visits by algorithm:
  – clinical symptoms (control), versus
  – FENO concentrations (intervention), with uptitration
    (>29 ppb) or downtitration (<16 ppb) of ICS dose

• Primary outcome: total asthma exacerbations
• ANZCTR 12607000561482

Powell, Lancet 2011

FENO-guided Care & Asthma Exacerbations

Powell, Lancet 2011
Summary

- **Menarche:**
  - ↑ BHR during perimenstrual & periovulatory phases
  - Early menarche associated with ↑ adult-onset asthma

- **Menopause:**
  - In at least some women, menopausal transition associated with ↑ adult-onset asthma
  - Menopausal asthma has ↑ sputum neutrophils

- **Pregnancy:**
  - Effect of pregnancy on asthma merits investigation
  - $F_E$NO-guided care may help achieve asthma control