

## Asthma in Adults: A Breathless Update

LTC Douglas Maurer, DO, MPH, FAAFP

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## LTC Douglas Maurer, DO, MPH, FAAFP

Program Director, Faculty Development Fellowship, Madigan Army Medical Center, Tacoma, Washington; Associate Professor, Uniformed Services University of the Health Sciences, Bethesda, Maryland; Clinical Associate Professor, University of Washington School of Medicine, Seattle.

LTC Maurer is a graduate of the Ohio University Heritage College of Osteopathic Medicine, Athens, and completed his family medicine residency at Tripler Army Medical Center, Honolulu, Hawaii. He earned a Master of Public Health (MPH) degree at the University of Washington, Seattle, and completed faculty development fellowships in Waco, Texas, and at Madigan Army Medical Center, Tacoma. LTC Maurer served for five years as program director of the Carl R. Darnall Army Medical Center (CRDAMC) Family Medicine Residency in Fort Hood, Texas. He currently practices full-service family medicine with a diverse patient population at Madigan Army Medical Center. Having taught medicine for nearly 20 years, LTC Maurer has won multiple teaching awards, including the 2015 Teacher of the Year award at Madigan Army Medical Center. His research interests include medical simulation, medical apps, student interest in primary care, prevention of obesity, and evidence-based medicine.

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## Learning Objectives

1. Reviewed current NHLBI asthma guideline.
2. Discussed new EIB guideline.
3. Evaluated latest evidence for asthma treatment.
4. Discussed prevention of asthma.
5. Reviewed some asthma in pregnancy pearls.

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## Audience Engagement System

The image shows three sequential screenshots of the Audience Engagement System app. Step 1 is the home screen with various icons for navigation. Step 2 shows a list of CME activities with a red arrow pointing to a specific activity. Step 3 shows the details of that activity, including the title 'CME011 Asthma: Current Synthesizing: Unchain My Heart' and a description.

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## Disclosures

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How many asthma patients do you see?

How do you normally treat them?

How comfortable are you treating them?

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## Practice Recommendations

- No changes in current NHLBI asthma guideline
- New EIB guideline favors SABA's not LABA's
- Symptom-based ICS or SiT use may be "OK"
- Careful using LABA's (but don't stop them!)
- Don't use LRA's as monotherapy
- Asthma exacerbations tx same in pregnancy!

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## Current Guideline Review

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## AES Poll Question #1

Which of the following is the correct spirometry criteria to diagnose asthma?

- A. Non-reversible obstruction of at least 10% FEV1
- B. Reversibility of at least 12% in baseline FEV1
- C. Reversibility of at least 5% in baseline FEV1
- D. Non-reversible obstruction of at least 20% FEV1

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## Asthma Diagnosis

- Reversibility: 12% in baseline FEV1 or 10% of percent predicted FEV1
- Methacholine challenge most sensitive test
- Positive: decrease in FEV1 > 20% at 8 mg/mL
- Decreased FEV1/FVC suggestive of dz
- Normal spirometry does not exclude asthma!

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## Risk Factors for Asthma

- Wheezing before age 3 years
- Atopy, allergic rhinitis
- Environmental: tobacco smoke, pets, gas cooking, mold, cockroach, dust-mites, cleaning, farming
- Perinatal: preterm delivery, maternal smoking
- Respiratory infections early in life
- Meds: aspirin/NSAIDS (sensitivity only), acetaminophen?
- Other: genetics, day care, overweight/obesity

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## Acute Asthma Treatment

- SABA's drug of choice for acute exacerbations
- Systemic corticosteroids reduce relapse, hospitalization, and SABA use
- Initial treatment: O2, SABA's, ipratropium bromide, and systemic corticosteroids\*
- Severe exacerbations: IV magnesium or heliox

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## Chronic Asthma Treatment

- 4 categories:
  - Mild intermittent
  - Mild persistent
  - Moderate persistent
  - Severe persistent

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## AES Poll Question #2

First line maintenance therapy for mild persistent asthma is which ONE of the following?

- Short acting beta agonists (SABA)
- Long acting beta agonists (LABA)
- Oral Prednisone
- Inhaled corticosteroids (ICS)
- Leukotriene receptor antagonists (LRA)

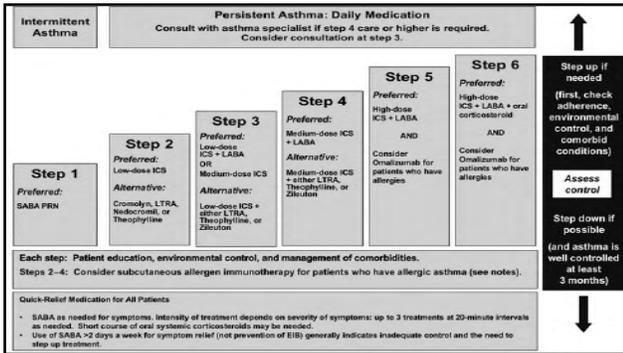
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## Chronic Asthma Treatment

- Stepwise treatment of categories
  - SABA only as needed for all categories
  - ICS preferred controller
  - LABA's preferred add-on agent after ICS
  - LRA's acceptable controller

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Components of Severity		Classification of Asthma Severity ≥12 years of age			
		Intermittent	Mild Persistent	Moderate Persistent	Severe Persistent
Impairment	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3-4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting beta <sub>2</sub> -agonist use for symptom control (not prevention of ERB)	≤2 days/week	>2 days/week but not daily, and not more than 1x on any day	Daily	Several times per day
Lung function	Normal FEV <sub>1</sub> /FVC, Interference with normal activity	None	Mild limitation	Some limitation	Extremely limited
	• Normal FEV <sub>1</sub> between exacerbations • FEV <sub>1</sub> >80% predicted • FEV <sub>1</sub> /FVC normal	• FEV <sub>1</sub> >80% predicted • FEV <sub>1</sub> /FVC normal	• FEV <sub>1</sub> >60% but <80% predicted • FEV <sub>1</sub> /FVC reduced >5%	• FEV <sub>1</sub> <60% predicted • FEV <sub>1</sub> /FVC reduced >5%	• FEV <sub>1</sub> <60% predicted • FEV <sub>1</sub> /FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0-1/year (see note)	≥2/year (see note)		
		Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. Relative annual risk of exacerbations may be related to FEV <sub>1</sub> .			
Recommended Step for Initiating Treatment (See "Stepwise Approach for Managing Asthma" for treatment steps.)		Step 1	Step 2	Step 3	Step 4 or >
		In 2-6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.			



1. In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school or at home?	SCORE
All of the time [1]      Most of the time [2]      Some of the time [3]      A little of the time [4]      None of the time [5]	.....
2. During the past 4 weeks, how often have you had shortness of breath?	.....
More than once a day [1]      Once a day [2]      3 to 6 times a week [3]      Once or twice a week [4]      Not at all [5]	.....
3. During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?	.....
4 or more nights a week [1]      2 or 3 nights a week [2]      Once a week [3]      Once or twice [4]      Not at all [5]	.....
4. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?	.....
3 or more times per day [1]      1 or 2 times per day [2]      2 or 3 times per week [3]      Once a week or less [4]      Not at all [5]	.....
5. How would you rate your asthma control during the past 4 weeks?	.....
Not controlled at all [1]      Poorly controlled [2]      Somewhat controlled [3]      Well controlled [4]      Completely controlled [5]	.....

If your score is 19 or less, your asthma may not be as well controlled as it could be. No matter what your score is, share the results with your healthcare provider. TOTAL: .....

## Severe Asthma

- Definition:
  - Requires high-dose ICS PLUS second agent OR
  - Oral steroids for ≥ 50% of previous year
- Eval and tx comorbidities: sinusitis, polyps, GERD, OSA, obesity, smoking, etc.
- Consider steroid resistance and eosinophilia
- Tx with ICS/LABA plus low dose theophylline or tiotropium or omalizumab

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## AES Poll Question #3

Treatments for exercise induced bronchoconstriction (EIB) include which of the following EXCEPT?

- Short acting beta agonists (SABA)
- Long acting beta agonists (LABA)
- Cromolyn
- Ipratropium bromide
- Leukotriene receptor antagonists (LRA)

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## Exercise-Induced Bronchoconstriction

- Formal postexercise spirometry for diagnosis
- SABA 15 min prior to exercise
- Alternant: mast cell stabilizer, anticholinergic
- NO LABA's!
- If use SABA daily: ICS or LRA
- Nondrug: warm up first, use mask or scarf

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## Latest Evidence on Acute Asthma Management

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## ER Management

- Nebulizers no better than MDI's via spacer
- Inhaled mag sulfate: no benefit; stick with IV
- Ketamine showed NO benefit in it's only RCT
- Weak data for IV beta agonists + inhaled
  - NO benefits for adults
  - Limited evidence in children

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## ER Management

- ICS in the ER for acute exacerbations
  - Reduced admissions if not treated with oral or IV
  - May reduce admissions when added to systemic
- Increasing ICS as part of an action plan ineffective
- Choice of oral steroid?
  - Prednisone vs. dexamethasone

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## Latest Evidence on Chronic Asthma Management

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## Symptom-Based ICS?

- Govt funded nonblinded RCT with 342 participants
- Randomized into 3 groups:
  - Physician adjusted based on 2007 guideline
  - Biomarker adjusted based on exhaled nitric oxide
  - Symptom-based ICS matched puff to puff to SABA
- Symptom-based group with similar outcomes
- Used half the dose of steroids as the other groups
- 2015 Cochrane: less steroid, no loss of control
  - Mild asthma patients only, need more studies

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## Single Inhaler Therapy (SiT)

- Combo formoterol/budesonide (SiT)
- 4 studies of over 9000 patients; no children < 12
- All industry funded
- SiT reduced:
  - Asthma exacerbations requiring oral steroids
  - ER visits and hospitalizations
  - Adverse events unclear
- NNT 100 to prevent admission or ER visit

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## ICS plus LABA...Right Away?

- Cochrane Review of 27 trials, 8050 participants
- RCT's comparing ICS + LABA with ICS alone
- Combo ICS/LABA no better than ICS alone
- Higher dose ICS superior to add on LABA
- Children responded similarly to adults
- No difference in adverse events

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## ICS plus LABA... Then Again...!

- 2016 industry funded RCT, 11,751 pts, > 12 yrs
- All patients with moderate-severe asthma
- Fluticasone vs fluticasone-salmeterol BID
- Primary outcome: first severe asthma exacerbation
- Combo reduced exacerbations more than ICS alone (8% vs 10%, NNT = 50 over 26 wks)
- No difference in intubations or deaths

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## When to Stop a LABA?

- Black box: stop LABA once asthma controlled
- Meta-analysis: 5 studies, 1292 pts says “No”
  - Patients did WORSE after stopping LABA
  - Lots of drop-outs due to poor control
- 2015 Cochrane: temporary loss of control

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## How to Stop a LABA?

- Prescriber’s Letter recommends:
  - Step up tx, go to medium ICS before LABA
  - Step down tx, go to lower dose of combo first
  - Stop LABA, keep ICS same or double dose
  - Still symptomatic, restart combo ICS/LABA

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## Risks of LABA’s

- Cochrane Reviews of LABA safety
  - 6 deaths in combo formoterol vs. 1 in ICS alone
  - No difference in non-fatal events
  - Salmeterol deaths all occurred with drug alone
  - No diff in head to head comparisons
- Ongoing FDA surveillance studies...

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## Adult Height and ICS

- Risks appear mild; still concern about height
- Govt funded RCT of 1000 children ages 5-13
- Treated with ICS, nedocromil or placebo for 4.3 yrs then enrolled in follow-up study
- Height measured in adulthood (mean age 25)
- ICS caused modest height reduction of 1.2 cm
- Most pronounced in girls

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## LRA as Monotherapy?

- Industry study: LRA’s “equivalent” to ICS/LABA
  - Outcomes DOE’s not POEM’s
  - All “improvements” gone by 2 years
- Cochrane: 65 studies, 10K adults, 3K children
  - LRA’s more asthma exacerbations (NNH 28)
  - LRA’s more dropouts for poor control (NNH 31)
- LRA ONLY as add on to ICS and LABA

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## New Asthma Treatments

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## Tiotropium for Asthma?

- 2012 industry funded RCT (N=900)
  - All with asthma not controlled on LABA or ICS
  - DOE improvements of pulmonary function
  - POEM decrease in exacerbations
    - 1 less exacerbation after 8 yrs of treatment!
- Multiple Cochrane Reviews in 2014/2015
  - LAMA add on therapy improves lung function
  - No difference in exacerbations of LAMA vs. LABA\*\*

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## Omalizumab

- 2013 Cochrane Review found omalizumab:
  - Reduces asthma exacerbations
  - Reduces hospitalizations
  - Well tolerated
  - Reduce/withdraw steroids
- Adjunct to ICS and steroid tapering
- FDA approved for ages 6 + with pos skin test
- Expensive! One vial: \$826!

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## Dupilumab

- Monoclonal antibody targeting IL-4Ra
- 104 adults, 18 -65 years, persistent asthma
- Randomized to dupilumab or placebo x 16 wks
- Decreased exacerbations when ICS and LABA tapered off BUT no difference as add-on tx!
- Not yet FDA approved

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## Bronchial Thermoplasty

- Only FDA approved nondrug asthma therapy
- Tube with four RF wires that destroy excess smooth muscle via bursts of heat
- One study showed 78% decrease in ER visits!
- Risk of exacerbation from procedure itself!
- Reserved only for severe asthmatics not controlled on ICS and LABA

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## Prevention

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## Asthma Action Plans (AAP)

- 2013 Cochrane: 13 RCTs (N=2,157), age > 17, ER visit received AAP
  - Decreased hospitalization, but not ER visits, quality of life or peak flow
- 2008 Cochrane: 36 RCTs, age > 16, evaluated PEF or symptoms plus AAP vs usual care
  - Decreased hospitalization, ER visits, missed work/school

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## AES Poll Question #4

Which of the following has been associated with the prevention of asthma and/or asthma exacerbations?

- Probiotics
- Influenza vaccine
- Vitamin C
- Nuts
- All of the above

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## Influenza Vaccine

- 2013 Cochrane Review of 18 trials
  - No reduction in influenza-related exacerbations
  - No apparent risk from inactivated vaccine
  - No risk from live intranasal influenza vaccination
  - Vaccines do not worsen asthma
- Insufficient evidence to determine if asthma attacks prevented by influenza vaccination

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## Asthma and Supplements

- Probiotics during pregnancy or early infancy do not prevent asthma
  - Meta-analysis of 20 RCTs included 4866 children
  - Various combinations/doses of probiotics
  - Followed children from 2 to 6 years after birth
  - No evidence of benefit
- Vitamin C not beneficial in asthma
  - 9 studies, 330 participants
  - One study with drop in FEV1 post-exercise

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## Asthma and Supplements

- Vitamin D does NOT prevent exacerbations in deficient patients
  - 250 pt RCT: vitamin D vs placebo; no difference in time to 1<sup>st</sup> exacerbation
- Caffeine improves airways function for up to four hours
  - 7 studies of 75 patients
  - Improved FEV1 by 12-18%
  - May need to avoid caffeine for at least four hours prior to spirometry

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## Nuts and Pregnancy

- Avoiding nuts during pregnancy controversial
- Danish Birth Cohort of 101,045 pregnancies
- Self-report data from validated questionnaire
- Nut intake inversely associated with asthma
- Consumption may decrease risk of allergies
- Nut consumption not harmful

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## AES Poll Question #5

Which of the following is the preferred controller agent for persistent asthma in pregnancy?

- A. Budesonide
- B. Albuterol
- C. Salmeterol
- D. Fluticasone
- E. Tiotropium bromide

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## Asthma and Pregnancy

- Asthma may improve, worsen or stay the same
  - Mild: 12.6% exacerbation/2.3% hospitalization
  - Moderate: 25.7%/6.8% **Smoking cessation!**
  - Severe: 51.9%/26.9%
- 15-20% increased risk of complications
  - Mortality, pre-e, preterm delivery, low birth weight
- Monitor peak flows bid +/- spirometry

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## Asthma and Pregnancy

- Medication safety
  - Albuterol (C), ICS (B/C), LABA (C), LRA (B), Ipratrop (B)
  - Carboprost (avoid!)
- “Best” data: albuterol, budesonide, salmeterol
- Less data: formoterol, LRA’s
- No diff in malformations b/t ICS vs. LABA/ICS
- Acute exacerbations in pregnancy tx’ed the same!

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## Practice Recommendations

- No changes in current NHLBI asthma guideline
- New EIB guideline favors SABA’s not LABA’s
- Symptom-based ICS or SiT use may be “OK”
- Careful using LABA’s (but don’t stop them!)
- Don’t use LRA’s as monotherapy
- Asthma exacerbations tx same in pregnancy!

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## Billing and Coding

- Asthma: J45.
  - Allergic (predominantly) asthma
  - Allergic bronchitis NOS
  - Allergic rhinitis with asthma
  - Atopic asthma
  - Extrinsic allergic asthma
  - Hay fever with asthma
  - Idiosyncratic asthma
  - Intrinsic nonallergic asthma
  - Nonallergic asthma

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## Billing and Coding

- Additional codes
  - Exposure to environmental tobacco smoke (Z77.22)
  - Exposure to tobacco smoke in the perinatal period (P96.81)
  - History of tobacco use (Z87.891)
  - Occupational exposure to environmental tobacco smoke (Z57.31)
  - Tobacco dependence (F17.-)
  - Tobacco use (Z72.0)

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## Billing and Coding

J45.2-	Mild intermittent asthma	Fifth character: 0, 1, 2
J45.3-	Mild persistent asthma	Fifth character: 0, 1, 2
J45.4-	Moderate persistent asthma	Fifth character: 0, 1, 2
J45.5-	Severe persistent asthma	Fifth character: 0, 1, 2
J45.9-	Other and unspecified asthma	
J45.90-	Unspecified asthma	Asthmatic bronchitis NOS Childhood asthma NOS Late onset asthma
J45.901	Unspecified asthma with (acute) exacerbation	
J45.902	Unspecified asthma with status asthmaticus	
J45.909	Unspecified asthma, uncomplicated	Asthma NOS
J45.99-	Other asthma	
J45.990	Exercise induced bronchospasm	
J45.991	Cough variant asthma	
J45.998	Other asthma	

## Billing and Coding

### When services performed in conjunction with:

Office Visit 992xx

99406-99407 Smoking and tobacco use cessation counseling (3-10 minutes, >10 minutes)  
G0436-G0437 Smoking and tobacco use cessation counseling, asymptomatic patient (3-10 minutes, >10 minutes) Medicare use codes

### Additional tests to confirm or monitor:

94010 Spirometry  
94060 Pulmonary function testing, pre- and post-  
+94729 DLCO  
Demonstration of aerosol generator, nebulizer, metered dose inhaler, or IPPB device  
94664  
94760 Pulse oximetry; single determination  
94761 ;multiple determinations (i.e., six-minute walk)  
94640 Nebulizer treatment

## Learning Objectives

- Reviewed current NHLBI asthma guideline
- Discussed new EIB guideline
- Evaluated latest evidence for asthma treatment
- Discussed prevention of asthma
- Reviewed some asthma in pregnancy pearls

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Questions?

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## Contact Information

LTC Douglas Maurer, DO, MPH, FAAFP

[douglas.m.maurer.mil@mail.mil](mailto:douglas.m.maurer.mil@mail.mil)

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## Associated Session

- Asthma in Adults: PBL

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