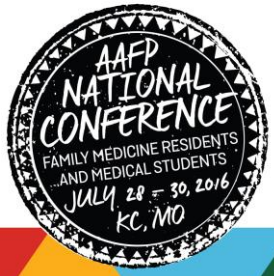

Disclosures

The views expressed are those of the author(s) and do not reflect the official policy of the Department of the Army, the Department of Defense or the U.S. Government.

How many asthma patients do you see?

How do you normally treat them?

How comfortable are you treating them?

Asthma: A Breathless Update

Douglas Maurer, DO, MPH, FAAFP
Program Director
Madigan Faculty Development Fellowship

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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Take Home Points

- 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

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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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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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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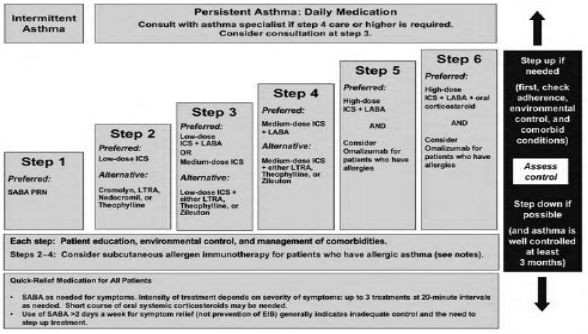
Components of Severity		Classification of Asthma Severity ≥12 years of age			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment Normal FEV_1/FVC: 8–19 yr 85% 20 –39 yr 80% 40 –59 yr 75% 60 –80 yr 70%	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3–4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily, and not more than 1x on any day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV_1 between exacerbations • FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 >60% but <80% predicted • FEV_1/FVC reduced 5%	• FEV_1 <60% predicted • FEV_1/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_1.			
Recommended Step for Initiating Treatment (See "Stepwise Approach for Managing Asthma" for treatment steps.)		Step 1	Step 2	Step 3	Step 4 or 5 and consider short course of oral systemic corticosteroids
		In 2–6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.			



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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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

ER Management

- Nebulizers no better than MDI's via spacer
- Inhaled magnesium 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 in patients not treated with oral or IV
  - May further reduce admissions when added to systemic
- Choice of oral steroid?
  - Prednisone vs. dexamethasone

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Latest Evidence on Chronic Asthma Management

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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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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When 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 dose same or double ICS dose
  - Still symptomatic, restart combo ICS/LABA

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Risks and Efficacy of LABA's

- Cochrane Reviews of safety of combo ICS/LABA vs. ICS alone and LABA vs. LABA
- Serious adverse events with all LABA's
  - 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 due to poor control (NNH 31)
- Stick with ICS for mild/mod persistent asthma
- LRA ONLY as add on to ICS and LABA

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New Asthma Treatments

Tiotropium for Asthma?

- Industry funded double blind RCT with 900 pts
  - 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
- Needs further study in peds populations
- 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

Influenza Vaccine

- 2013 Cochrane Review of 18 trials
  - Trial of 700 children demonstrated no reduction in influenza-related asthma exacerbations
  - No apparent risk from inactivated vaccine
  - 2 studies of live intranasal influenza vaccination demonstrated no risks of harm
- Insufficient evidence to determine if asthma attacks prevented by influenza vaccination
- Influenza vaccines do not worsen asthma

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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
- Vitamin D does NOT prevent exacerbations in deficient patients
  - 250 pt RCT: vitamin D vs placebo; no difference in time to 1st 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
- LOTS of logistic regression for confounders
- Nut intake inversely associated with asthma
- Nut consumption during may decrease risk of allergic disease in children
- Nut consumption not harmful

Asthma and Pregnancy

- Asthma may improve, worsen or stay the same
  - Mild: 12.6% exacerbation/2.3% hospitalization
  - Moderate: 25.7%/6.8%
  - Severe: 51.9%/26.9%
- 15-20% increased risk of complications
  - Perinatal mortality
  - Pre-eclampsia
  - Preterm delivery
  - Low birth weight
- Monitor peak flows bid +/- spirometry
- Smoking cessation!

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 major malformations b/t ICS vs. LABA/ICS
- Acute exacerbations in pregnancy tx'ed the same!

Asthma Cases

10 Minutes

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Questions?

Q&A

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