Asthma: It's New Day!

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Disclosures And Conflict Of Interest

• None

Outline

• History of asthma treatment
• Asthma “Stats” for Montana
• New Approaches to Treating Asthma
  • Optimization
  • Personalization
  • Lifestyle
When Were Asthma Medications Discovered?

- 1900: Epi and cortisone discovered (not used for years!)
- 1930: Epinephrine SQ
- 1955: Prednisone FDA approved
- 1956: Pressurized metered dose inhaler
- 1956-60s: Inhaled epinephrine (increased asthma deaths)
- 1960s: Albuterol
- 1970s: Inhaled steroids, theophylline, Cromolyn (Intal)
- 1990’s: Leukotriene modifiers (Singulair), LABA (Serevent)
- 2000: ICS/LABA (Advair)
- 2003: Omalizumab=anti-IgE (Xolair)
- 2015: LAMA (Spiriva) and mepolizumab (Nucala)

Are Montanans With Asthma Well Controlled? **NO**

- Est. 89,400 people in Montana have current asthma
- 52% of adults and 36% of children with asthma report sx's indicating asthma is not well/very poorly controlled
- 60% of adults & children with asthma report limiting their activities at least some because of asthma

Are Montanans With Asthma Well Informed? **NO**

- Only 65% of adults with asthma report knowing sx's of an asthma attack.
- Only 78% having been taught how to respond to an attack.
- Only 25% report having Asthma Action Plan to help make treatment decisions.
- Of a sample of children with uncontrolled asthma, only 26% were determined to have good inhaler technique
Is Treating Asthma in MT Expensive?

In 2014:
- $900 per ER visit; >2400 ER visits per year
- $8700 per hospital stay; 547 hospital stays per year
- Average length of stay: 1.9 days
- $3.6 million: est. total charge for ER visits for asthma

http://dphhs.mt.gov/asthma

What’s New In Asthma? Biomarkers

Sample: Sputum, breath, blood, BAL, urine

Identify:
- pts at risk for asthma attacks
- pts level of lung inflammation
- pts responsive to particular medications

Name Some Biomarkers for Asthma?

- Serum IgE: used for dosing omalizumab (Xolair)
- Sputum eosinophils: Gold std but technically difficult
- Blood eosinophils (>400): for anti-IL5 biologics
- FeNO: exhaled nitric oxide (breath analysis)
- Surfactant-D Chest 2016;149:1165
- Severe asthma: increased serum levels
- EPX (eosinophil peroxidase) in NP swab Allergy 2016, 71:567
  - Correlates with sputum eos; potential use in peds!
- Blood neutrophils: Eur Resp J 2016;48:976
  - Elevations correlate w/ asthma attacks & poor asthma control
What’s New In Asthma? Optimization
Take a current medication and make it better!

- Better delivery:
  - Smaller particles
  - Different propellant
  - Easier device to use

Has proper inhaler use increased?
- No, not in 40 years!

Is Using An Inhaler Easy? NO

- MDI
  - Poor actuation-inhalation coordination poor delivery suboptimal control
  - Error common: 1/3 to 2/3 of pt have poor coordination
  - >1 sec delay: 3-fold reduction in inhaled dose
  - Actuation during exhalation: 12-fold reduction

- DPI: need sufficient inspiratory flow

Optimization: Medication Delivery
Medication delivery Deposition in Lungs
- pMDI (pressurized metered dose inhaler)
  - Small particle vs. large particle
- DPI (Dry Powder Inhaler)
  - Proair RespIClick® (>4 yr)
- Nebulizer
  - Respimat® (slow moving mist): Spiriva®
Are There Once A Day Inhalers?
ICS/LABA: Fluticasone furoate/vilanterol (Breo Ellipta®)
LAMA: Tiotropium (Spiriva Respimat®)
(1.25 mcg) 2 puffs, add on for ≥12 y/o

Optimization: Education
• “Reactive Airways Disease” A Lazy Term of Uncertain Meaning That Should Be Abandoned”
• Make the right diagnosis
  • Use spirometry with bronchodilator (≥5 yrs old)
  • Assess individual circumstances
• Explain: risks of un-treated asthma vs risk of meds as well as benefits of medications
• Promote self-management and self-confidence
FAHY , and O'BRYNE Amer J Respir Crit Care Med. 2001; 163 (4): 822.

Personalization: What Does It Mean?
• Personalized medicine: medical model that separates pts into different groups with medical decisions, practices, interventions and/or products being tailored to the individual pt based on their predicted response or risk of disease.
Which 3 Novel Drugs Are Now Available For “Personalization” For Asthma Pts?

- **Blocks IgE**
  - **Anti-IgE** (Omalizumab=Xolair®) SQ q2-4 wks, ≥6 y/o
- **Affects Eosinophils**
  - **Anti-IL-5**: (works best if eos >400*)
    - Mepolizumab (Nucala®): SQ q4 wks, ≥12 y/o
    - Reslizumab (Cinqair®): IV q4 wks, ≥18 y/o

*Corren et al. Chest 2016:150;799

Which Novel Drug that blocks IL-4 and IL-13 May be Useful For Asthma and Eczema Pts?

- **Dupilumab**:
- **Asthma**:
  - RDBPC trial n=769 adults with mod-severe persistent asthma on ICS/LABA
  - Improved FEV1 and reduced exacerbations
- **Atopic dermatitis**: 2 phase 3 trials
  - Improved signs/symptoms including pruritus, symptoms of anxiety and depression and QOL compared with placebo.


New Drugs That Don’t Work For Asthma

- **Anti-CXCR2**
  - Pill that affects neutrophils/neutrophilic inflammation
  - Phase 2b clinical trial in adults: did NOT reduce asthma attacks compared to placebo
- **Anti-IL-13 monoclonal antibody (lebrikizumab)**
  - SQ injection monthly
  - Phase 3 trials in >2000 adults; did NOT consistently reduce asthma attacks

Does Lifestyle Make A Difference For Pts With Asthma?

- Diet
- Obesity
- GE reflux
- Vitamins
- Exercise

Yes

- Yoga
- Stress Relief
- Air pollution (indoor or outdoor)
- Vaccines

Does Diet Make A Difference In Asthma?

- Children who grew up eating "Mediterranean Diet" high in nuts and fruits (grape, tomato, apple) had less asthma symptoms. Mediterranean diet and childhood asthma. Allergologia et Immunopathologia. 2007;44 (2): 99.


Yes!

LIFESTYLE: DIET

Vitamin C and E, beta-carotene, flavonoids, magnesium, selenium, omega-3 fatty acids

lower rates of asthma

Foods high in carotenoids: carrot, watermelon, mango, tomato
Lifestyle: Obesity and GE Reflux

- **Obesity**:
  - Associated with severe asthma (ER visits) and decreased PFTs.
- **GE reflux**:
  - Associated with asthma symptoms. GE reflux is more likely if eat: too much, too fast, or too late at night. *Recent clinical investigations examining the association asthma and GE reflux.* Harding. *Am J Med.* 2003;115 Suppl 3A:39S.

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Which Vitamin can Help Asthma?

- **Vitamin D**:
  - Low Vitamin D: linked to asthma attacks and low lung function.
  - Vitamin D supplements may improve asthma control. *J Allergy Clinical Immunol, online June 10, 2010*

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Does Exercise Make Asthma Worse Or Better?

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<th>Worse</th>
<th>Better</th>
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<td>Common trigger of asthma (90%)</td>
<td>Improves QOL</td>
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<tr>
<td>More symptom free days</td>
<td>Better oxygen consumption</td>
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<td>Less inflammation</td>
<td>Help maintain healthy weight</td>
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How much exercise is enough? At least 30 min twice a week.
Can Yoga Improve Pulmonary Function In Asthma?

Yoga: kapalabhati = (high frequency breathing yoga technique)
- 60 adults with mild asthma
- kapalabhati vs deep breathing x 10 min
- Increase FEV1 by 200 mL
- Rapid and cost effective!

https://www.youtube.com/watch?v=sgfA57V68

Does Stress Trigger Asthma?

Pts with asthma who have anxiety and depression are at increased risk of asthma attacks!
- Psychological distress: rates higher in uncontrolled asthma
  - 24% in controlled asthma
  - 32% partially controlled asthma
  - 42% in uncontrolled asthma
- Vocal cord dysfunction (VCD): complicates asthma and does NOT respond to asthma meds.
  - Interventions: Counseling, breathing relaxation, anxiolytics

Eur Respir J. 2015;45:1557

Can Fixing Indoor Air Quality Improve Asthma? Yes

Allergens: dust mite, pet hair, mold, mice, cockroach
Smoke: cigarette, wood stoves/fire places
Fumes: gas stoves
Strong chemicals & fumes
- Dust mite encasements
- HEPA air filters
- Reduce asthma exacerbations
- Reduce symptoms

Yes
Does Outdoor Air Pollution Affect Lung Growth In Children?

- Cohort study in Boston from 1999-2002
- 8 yr follow up of 614 children: “geocoded” for location
- Results
  - PM2.5 affects lung growth (FVC) and obstruction (FEV1)
  - 50% reduction in lung growth if lives within 100 m
  - No effect if lives beyond 400 m from roadway
- Conclusion:
  - Living near a freeway may stunt lung volume growth in children

Which 2 Vaccines Are Recommended For Pts With Asthma?

- **Influenza**: recommended for all >6 mo old, but especially for those with asthma.
  - Egg allergy is **not** a contraindication to flu vaccine!
  - Intranasal flu vaccine is **not** effective for children!
- **Pneumococcal (PPSV23=Pneumovax)**
  - 2 to 64 y/o should get 1 dose of PPSV23: Chronic lung disease, including COPD, emphysema and **asthma**

https://www.cdc.gov/vaccines/vpd/pneumo/hcp/who-when-to-vaccinate.html

Conclusions

- History of asthma Tx: still using medication from 60 yrs ago (Prednisone)
- MT Stats: asthma is **not** adequately being managed
- New Approaches to Treating Asthma
  - **Optimization**:
    - Improve delivery to airways
  - **Personalization**:
    - Improve adherence (once a day)
    - Improve education (chronic disease)
    - Medication targets (IgE, IL-5, eos. IL-4/IL-13, neutrophils)
  - **Lifestyle**: It’s more than just medications!
New Paradigm For Treating Asthma

- Stay calm
- Quit smoking (and vaping)
- Live >400 m from highways
- Eat your veggies
- Maintain a healthy weight
- Exercise 30 min twice a wk
- Practice yoga
- Take Vitamin D
- Get vaccinated
- Treat your GE reflux
- Avoid allergic triggers
- Take your meds (correctly)
- Learn inhaler technique
- Check: IgE, CBC
- Monitor spirometry
- Regular follow up visits

Regular follow up visits