Updates to Asthma Guidelines and Exercise-Induced Asthma

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No Disclosures
Asthma Guidelines Update 2021 Overview: Introduction

- NAEPP EPR-3 2007
- Global Initiative for Asthma 2019/2020
- NAEPP 2020 Update
- Reconciling the Updates
- Diagnosing and Treating Exercise Intolerance
- All That Wheezes Is Not Asthma
Asthma Guideline Update 2021 Overview: Caveats and One Acknowledgement

- Today’s Information Applies (Mostly) To Children 5 Years of Age and Older
- Today, We Will Review Basic Options
- We Will Not Cover FeNO Nor Biologic Asthma Treatments
- Patients Not Reaching Desired Goals Following Initial Treatment Require Further Evaluation
- Appreciation to Dr. T. Bernard Kinane (MGH) for discussion re. exercise bronchoconstriction in winter athletes
Respecting the Guidelines

National Institutes of Health
National Asthma Education Prevention Program (NAEPP)

2007 Guidelines for the Diagnosis and Management of Asthma (EPR-3)

http://www.nhlbi.nih.gov/guidelines/asthma/index.htm
Guidelines: They Work

- I assume you know them
- EPR-3 assumes asthma is the same illness in most ages
- Providers categorize **Severity** at diagnosis
  - Intermittent, mild, moderate, severe
- Providers' assessment of **Control** includes impairment, risk, and spirometry
Why Asthma Guidelines Fail

• Asthma is a non-uniform, developmental illness
• Birth – Two: The happy wheezer
• Ages two – six: Early Asthma
• Ages 6 and older: Chronic disease
• “...Consider childhood asthma as a developmental disease...as a condition in which the basic abnormality consists of an altered development of immune and airway response to external stimuli....”
  – Fernando Martinez, Pediatric Respiratory Medicine, 1999
The Tucson prospective longitudinal study showed that most children under the age of 3 years who wheeze do not have asthma, but, rather, have “transient early wheeze” due to virus.

Bruce K Rubin, and Jeffrey M Haynes Respir Care 2012;57:1314-1324 adapted from Martinez, 1995.

(c) 2012 by Daedalus Enterprises, Inc.
Bristol Model of Asthma Phenotypes in Children 6-81 Months

**Figure 1** Estimated prevalence of wheezing at each time point from birth to 81 months for each of the six wheezing phenotypes identified by latent class analysis in 6265 children with complete data.

Bristol Model of Asthma Phenotypes in Children 6-198 months

Global Initiative for Asthma (GINA)

What's new in GINA 2020?

GINA Global Strategy for Asthma Management and Prevention
A reminder – the key change in GINA 2019

GINA 2019: a fundamental change in asthma management

Treatment of asthma with short-acting bronchodilators alone is no longer recommended for adults and adolescents


@ERSpublications
GINA no longer recommends treating adults/adolescents with asthma with short-acting bronchodilators alone. Instead, they should receive symptom-driven (in mild asthma) or a daily corticosteroid-containing inhaler, to reduce risk of severe exacerbations. http://bit.ly/310LLzE

The 2019 Global Initiative for Asthma (GINA) treatment strategy figure for adults and adolescents, annotated to highlight key features.

Exercise Intolerance, Exercise-Induced Asthma, and Exercise-Induced Bronchospasm

WHERE PATIENTS PRESENT WITH SYMPTOMS

On the racetrack
On the short track
  On the rink
In the water
On the field
  On an erg
On the block/In the blocks
At the barre
On the stage
We Care About Exertional Dyspnea Because It is Common

Asthma based on combined criteria

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Subjects</th>
<th>Prevalence [95 % CI]</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Larsson et al. [19]</td>
<td>1993</td>
<td>42</td>
<td>55 % [39–70 %]</td>
<td>23.37 %</td>
</tr>
<tr>
<td>Sue-Chu et al. [22]</td>
<td>1996</td>
<td>171</td>
<td>21 % [15–28 %]</td>
<td>26.52 %</td>
</tr>
<tr>
<td>Michalak et al. [23]</td>
<td>2002</td>
<td>180</td>
<td>14 % [10–20 %]</td>
<td>26.58 %</td>
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<tr>
<td>Turmel et al. [25]</td>
<td>2012</td>
<td>44</td>
<td>30 % [17–44 %]</td>
<td>23.53 %</td>
</tr>
<tr>
<td>Overall (I^2 = 92.35%, p &lt; 0.001)</td>
<td>437</td>
<td></td>
<td>28 % [13–46 %]</td>
<td>100.00%</td>
</tr>
</tbody>
</table>

Definitions

Exercise-Induced Asthma

- Asthma exacerbated rather than caused by exertion
- Occurs in individuals with documented asthma
- Decreased symptoms with ICS
- 90% of adults with POS Methacholine challenge
- Eosinophilic inflammation predominates

Adapted from Weiler, J, et al. J Allergy Clin Immunol 2016;138:1292-5.)
Definitions

Exercise-Induced Bronchoconstriction

- Reduced lung function transiently with exercise
- Occurs in individuals without documented asthma
- Not blocked by ICS alone
- 75% of adults with NEG Methacholine challenge
- Airway neutrophils predominate

So What Causes Bronchospasm in Exercise? Exertion in cold, dry air worsens FEV1 compared to exercise in warm, dry air.

Greater intrathoracic water loss is associated with increased bronchospasm

Breathing warm, moist air after exertion in dry air does NOT lead to excessive bronchospasm.

Exercise-induced bronchoconstriction is the result of airway smooth muscle contraction due to breathing dry air, exacerbated at cold temperatures, and without worsening with rewarming. Inflammatory mediator release is associated with this process.

Inflammatory Markers Exist in Athletes Even Without Asthma

Inflammatory mediators in EIB

So How Does One Treat EIA?

Bronchial Hyperresponsiveness *in asthmatics* improves with inhaled steroid therapy and there may be a (weak) role for LTRAs.

## Effects of Common Anti-Asthma Medications on Exercise-Induced Asthma

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose (puffs)</th>
<th>Timing before exercise (min)</th>
<th>Effectiveness*</th>
<th>Duration of protection (hr)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>β2 Aerosols</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salmeterol‡</td>
<td>2</td>
<td>10–15</td>
<td>+++</td>
<td>10–12</td>
</tr>
<tr>
<td>Albuterol</td>
<td>2</td>
<td>10–15</td>
<td>+++</td>
<td>2.0–2.5</td>
</tr>
<tr>
<td>Terbutaline</td>
<td>2</td>
<td>10–15</td>
<td>+++</td>
<td>2.0–2.5</td>
</tr>
<tr>
<td>Cromolyn sodium</td>
<td>2</td>
<td>10–15</td>
<td>++</td>
<td>1.5–2.0</td>
</tr>
<tr>
<td>Nedocromil sodium</td>
<td>2</td>
<td>10–15</td>
<td>++</td>
<td>1.5–2.0</td>
</tr>
<tr>
<td>Methylxanthines</td>
<td>Variable</td>
<td>30–60</td>
<td>+/-</td>
<td>?</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>2</td>
<td>30–60</td>
<td>+/-</td>
<td>?</td>
</tr>
</tbody>
</table>

Therapy for EIB: Warm Up!

Warming up induces a refractory period for bronchoconstriction equally well with a 10-15 minute low intensity jog.

- 8 30-sec runs on a treadmill,
- 45-sec recovery between each sprint.
- Peak Velocity

Therapy for EIB: Mask Up!

Options for Treatment of EIB

- Albuterol 10-30 minutes before exertion
- PLUS Warmup 30 minutes before exertion
- Plus Mask! Especially for winter athletes

- Role for LAMA

- Weak Role for LTRA (montelukast)

- Combined ICS/LABA (SMART)

What Is It If It Isn’t Asthma? Examples

Semantics Matter:
• Vocal Cord Dysfunction
• Exercise-Induced Laryngeal Obstruction
• Psychogenic Stridor

Role of Treadmill Exercise Testing:
• Low Yield Without Maximal Effort
• Reduces But Does Not Exclude Risk of Asthma
• Requires Caution Without Concurrent Laryngoscopy!!

Vollstaeter, M et al. Spirometry - a tool for diagnosing exercise induced laryngeal obstruction (EILIO)? European Respiratory Journal 2014 44: P4874
What Is It If It Isn’t Asthma?  Examples

• VCD/EILO  

Dynamic Hyperinflation
Diagnostic and Treatment Algorithm in Patients with Symptoms Suggestive of EIA/EIB

Patient with symptoms of exercise intolerance

↓

Spirometry

FEV1/FVC < LLN?

↓

Treat for Obstructive Disease/EIA

↓

If FEV1/FVC improved with persisting sx, consider exercise bronchoprovocation

↓

FEV1 decrement > 15%?

↓

Maximize pre-exercise treatment

Increase Asthma Step Therapy

FEV1/FVC ≥ LLN

↓

Exercise bronchoprovocation FEV1 drop > 15%?

Yes

No

Treat for EIB

Consider Other Dx

FEV1 decrement > 15%?

VCD/EILO

GER

Anxiety

Dynamic Hyperinflation

Are you still with me?
All That Wheezes Is Not Asthma

Swedish Pediatric Breathing Program
Swedish Flexible Bronchoscopy Program
Swedish Aerodigestive Program incorporating Gastroenterology and Otolaryngology

206-215-2700
Thank You!

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