Exercise and Asthma: What patients and doctors can do to improve outcomes

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Conflicts of Interest

Research
• Novartis
• GSK
• Forest
• Genentech
• Merck

Speaker
• Teva
• Merck
Objectives

1. To understand the physiology of EIB
2. To be able to diagnose EIB
3. To successfully treat EIB
4. To understand that patients with asthma avoid exercise
5. Demonstrate the importance of exercise in mice and humans with asthma
Changes in FEV1 Before & After 8 minutes Cycling Exercise in 27 adult asthmatics

What causes EIB?

- A. Hot humid air
- B. Cold air
- C. Dry air
- D. Ozone
- E. Both cold and dry air

Ans:
What causes EIB:

- A. Hot humid air
- B. Cold air
- C. Dry air
- D. Ozone
- E. Both cold and dry air

Ans: C
RHE = Respiratory Heat Exchange

Inflammatory Cells in sputum with EIB

FIG 3. Comparison of the concentration of columnar epithelial cells (A) and the concentration of eosinophils (B) in induced sputum between asthmatic subjects with EIB and asthmatic control subjects without EIB. The median concentration of columnar epithelial cells and eosinophils was higher in the group with EIB.

Hallstrand et al, JACI 2005;116:586-593
Inflammatory mediators in EIB

Histamine (ng/ml) $P = 0.001$
Tryptase (ng/ml) $P = 0.003$
CysLT (pg/ml) $P = 0.021$

Curr Opin Allergy Clin Immunol 2006,6:37-42
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DIFFERENTIAL DIAGNOSIS FOR EIB

- Asthma
- Pulmonary diseases other than asthma: bronchitis, pneumonia, emphysema, pulmonary embolism, CF, croup, bronchiolitis
- GE reflux
- Anaphylaxis
- Severe nasal congestion
- Laryngeal dysfunction, VCD
- Carcinoid tumor
- Cardiac
- Poor conditioning

What percent of children with dyspnea will have EIB on exercise challenge test?

• A. 1
• B. 11
• C. 55
• D. 85
• E. 95

• Ans:
What percent of children with dyspnea will have EIB on exercise challenge test?

- A. 1
- B. 11
- C. 55
- D. 85
- E. 95

Ans: B
Percent diagnosis of 117 children with exercised induced dyspnea diagnosed by treadmill

- Physiologic: 74%
- VCD: 13%
- EIB: 11%
- Restrictive: 13%
- Other: 13%

Weinberger et al 2008
Is the history of EIB reliable in athletes?

- A. No
- B. Yes
Is the history of EIB reliable in athletes?

- A. No
- B. Yes

Answer: no
Exercise challenge Results in Athletes with Symptoms of EIB
Evaluation:

- Detailed history and exam
- Prevented by albuterol before exercise.
- PFT pre and post beta-agonists
- Challenge test, but what type?
  - free run
  - controlled exercise challenge
  - surrogate challenge
## Exercise Challenge: external source dry air

<table>
<thead>
<tr>
<th>Step</th>
<th>Duration</th>
<th>Target HR</th>
<th>Treadmill Rate</th>
<th>Treadmill Incline</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2 minutes</td>
<td>50% MHR</td>
<td>2.5 mph</td>
<td>0%</td>
</tr>
<tr>
<td>2</td>
<td>2 minutes</td>
<td>70% MHR</td>
<td>increase</td>
<td>increase</td>
</tr>
<tr>
<td>3</td>
<td>6 minutes</td>
<td>&gt;80% MHR</td>
<td>increase</td>
<td>increase</td>
</tr>
</tbody>
</table>
Positive test

- Adequate test is 8 minutes with >80% MHR achieved in 2 minutes, with 6 minutes at MHR
- Ventilation should be 40-60% MVV
- Positive EST: symptoms with 10% or more drop in FEV-1
- If negative on treadmill do a “in venue challenge” in children or surrogate test for adults
% fall in FEV1 after exercise in relation to PD15 to mannitol

Brannan et al, AJRCCM 1998; 158:1120-6
Relationship of sensitivity to EVH & sensitivity to 4.5% saline

Smith CM & Anderson SD Eur Respir J 1989; 2: 36-43
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The effect of inhaled corticosteroids on EIB is?

• 1. not effective to eliminate EIB
• 2. reduces EIB by 10%
• 3. reduces EIB by 25%
• 4. reduces EIB by 50%
• 5. reduces EIB by greater than 75%

• Ans:
The effect of inhaled corticosteroids on EIB is?

- 1. not effective to eliminate EIB
- 2. reduces EIB by 10%
- 3. reduces EIB by 25%
- 4. reduces EIB by 50%
- 5. reduces EIB by greater than 75%

Ans: 5
Effect of progressive doses of ICS on EIA

Average attenuation of EIA was 30% for all doses, but with 25% in low doses and 50% in higher doses of qd ciclesonide, compared to up to 65 to 80% in other bid studies.

Subbarao. JACI 2006; 117: 1008
Regular Use of Beta-agonists May Lead to Increased EIB

Comparing salmeterol, formoterol and terbutaline for EIA by change in % FEV-1 over time

Richter. Eur Resp J. 2002; 19; 865
Placebo’s effect on % of patients responding post albuterol in minutes at week 0, 1 and week 4

Montelukast’s effect on % of patients responding post albuterol in minutes at week 0, 1 and week 4

Salmeterol’s effect on % of patients responding post albuterol in minutes at week 0, 1 and week 4
Effect of ipratropium bromide on EIA

All three arms had a 16% drop in FEV1 with exercise

FEV₁ as percentage of initial value (%)
Assessing effect of Nedocromil (NCS) and Cromolyn (SCG) on EIB

Max % decrease in FEV1

No significant difference in post exercise FEV1, complete protection or clinical protection between NCS and SCG

Kelly. Eur Resp J 2001; 17: 39
Comparing salmeterol, montelukast, zileutin and placebo in change of FEV1 over hours after exercise

No difference between montelukast, zafirlukast or salmeterol, but zileutin at 8 and 12 hours was less effective

Coreno et al. JACI. 2000: 106; 500-6
Other Therapies

- Warming up
- Salt restriction
- Hydration
- Fish oil
- Magnesium
- Anti-oxidants vitamins

- Alternative therapies should not replace traditional therapies since data supporting their use are limited.
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Impact of Health on Activities

Q2a. Does your health keep you from going to school or working?
Q2b. Are you limited in the kind or amount of work you can do because of your health?
Q2c. Are your activities limited in any way by your health?

Base: Adult cross-section

- Keep from school/work: 26% (Asthma) 9% (Non-Asthma)
- Limited in work: 18% (Asthma) 8% (Non-Asthma)
- Limited in any way: 12% (Asthma) 5% (Non-Asthma)
- Not limited: 78% (Non-Asthma)

Asthma Adults, N = 86  Non-Asthma Adults, N = 999
What % of Children with asthma admitted that asthma interfered with participation in school sports?

- A. 10
- B. 26
- C. 50
- D. 76
- E. 90

Answer:
What % of Children with asthma admitted that asthma interfered with participation in sports?

- A. 10
- B. 26
- C. 50
- D. 76
- E. 90

Answer: B
Q22a. Are there any activities that you would like to do, but avoid doing because of coughing, wheezing, shortness of breath after exercise, play or exertion?

Base: Asthma patients that experience symptoms DURING OR SHORTLY AFTER exercise
Health Limits Activities: A Lot or Some

Q49. How much do you feel that your health limits what you can do in each of the following areas. Do you feel your health restricts you – a lot, some, only a little or not at all in....
Base: Adult cross-section
Q55. As a result of your asthma, how often do you feel . . . ? Often, sometimes, rarely, or never?

Base: All Asthma Patients, Unweighted N=1,517
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What is the importance of exercise in the mouse model with asthma
Effect of exercise on inflammatory mediators of asthma

Pastva. J Immunol 2004;172;4520-4526
IgE production in sedentary and exercising mice

Pastva. J Immunol 2004;172;4520-4526
Exercise decreased VCAM-1 surface expression in the lungs of OVA-sensitized mice
IL-4 (pg/ml) vs IL-5 (pg/ml)

- Sedentary, OVA
- Exercised, OVA

Pastva. J Immunol 2004;172;4520-4526
The number of total cells, eosinophils and epithelial cells in the bronchoalveolar lavage
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Exercise Improves Asthma Outcomes  
“Quality of Life”

<table>
<thead>
<tr>
<th></th>
<th>Control Group</th>
<th>Exercise Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline (n=12)</td>
<td>Baseline (n=18)</td>
</tr>
<tr>
<td><strong>ACQ Questionnaire</strong></td>
<td>0.90±0.15</td>
<td>1.30±0.19</td>
</tr>
<tr>
<td><strong>ACQ with Spirometry</strong></td>
<td>1.06±0.10*</td>
<td>1.37±0.21</td>
</tr>
<tr>
<td><strong>Perceived Asthma Control</strong></td>
<td>2.33±0.19</td>
<td>2.56±0.15</td>
</tr>
<tr>
<td><strong>Mini-AQLQ</strong></td>
<td>5.79±0.15</td>
<td>5.01±0.21</td>
</tr>
<tr>
<td><strong>Maximal VO₂</strong></td>
<td>2.66±0.27</td>
<td>2.63±0.20</td>
</tr>
<tr>
<td><strong>Submaximal Vₑ/VO₂</strong></td>
<td>23.21±0.73</td>
<td>24.89±1.08</td>
</tr>
<tr>
<td><strong>Maximal Vₑ/VO₂</strong></td>
<td>28.46±0.88</td>
<td>28.84±1.02</td>
</tr>
<tr>
<td><strong>Submaximal DI</strong></td>
<td>0.42±0.03</td>
<td>0.45±0.02</td>
</tr>
<tr>
<td><strong>Maximal DI</strong></td>
<td>0.68±0.04</td>
<td>0.73±0.04</td>
</tr>
</tbody>
</table>

ACQ: Asthma Control Questionnaire; AQLQ: Asthma Quality of Life Questionnaire; VO₂: Oxygen uptake; Vₑ: Ventilation; DI: Dyspnea Index

¹n=12 for paper measurements only; ²n=17 for paper measurements only; ³significant differences at baseline between control and exercise group; ⁴p<0.05 between groups from T1 to T2; ** p<0.05 within exercise group from T2 to T3; ***p<0.05 within exercise group from T1 to T3; ^ statistical trend from T1 to T2; p<0.10.

Dogra. ERJ June 7, 2010
Exercise Improves Asthma Outcomes

“Symptom Free Days”

Mendes. CHEST / 138 / 2 / AUGUST, 2010
Exercise Improves Asthma Outcomes

“Oxygen consumption”

Mendes. CHEST / 138 / 2 / AUGUST, 2010
## Exercise in children: all compared to open label conventional treated group

<table>
<thead>
<tr>
<th>author</th>
<th>duration</th>
<th>frequency</th>
<th>type</th>
<th>P value</th>
<th>Subject #</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basaran 2006</td>
<td>2 months</td>
<td>1 hour, 3X a week</td>
<td>Aerobic, moderate</td>
<td>0.001</td>
<td>62</td>
</tr>
<tr>
<td>Fanelli 2007</td>
<td>4 months</td>
<td>1.5 hours, 2X a week</td>
<td>Aerobic to 70%</td>
<td>0.03</td>
<td>38</td>
</tr>
<tr>
<td>Flapper 2008</td>
<td>3 months</td>
<td>2.5 hours, 1 time a week</td>
<td>Aerobic</td>
<td>0.02</td>
<td>36</td>
</tr>
<tr>
<td>Moreira 2008</td>
<td>3 months</td>
<td>50 minutes, 2X weekly</td>
<td>Aerobic</td>
<td>0.004</td>
<td>34</td>
</tr>
</tbody>
</table>

D. Pacheco, J of Asthma, 2012
**Exercise in adults: all compared to open label conventional treated group**

<table>
<thead>
<tr>
<th>author</th>
<th>duration</th>
<th>frequency</th>
<th>type</th>
<th>P value Subject #</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turner 2010</td>
<td>6 weeks</td>
<td>1.5 hour, 3X a week</td>
<td>Aerobic, moderate</td>
<td>0.04 34</td>
</tr>
<tr>
<td>Goncalves 2008</td>
<td>3 months</td>
<td>0.5 hours, 2X a week</td>
<td>Aerobic to 70%</td>
<td>0.001 20</td>
</tr>
<tr>
<td>Mendes 2010</td>
<td>3 months</td>
<td>0.5 hours, 2X a week</td>
<td>Aerobic to 70%</td>
<td>0.001 101</td>
</tr>
</tbody>
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D. Pacheco, J of Asthma, 2012
## Exercise in Adults, non aerobic: all compared to open label conventional treated group

<table>
<thead>
<tr>
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<th>duration</th>
<th>frequency</th>
<th>type</th>
<th>P value Subject #</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sabina 2005</td>
<td>1 month</td>
<td>1.5 hour, 2X a week</td>
<td>Yoga</td>
<td>NS 62</td>
</tr>
<tr>
<td>Thomas 2009</td>
<td>1 and 6 months</td>
<td>3 sessions</td>
<td>Breathing exercises</td>
<td>NS 183</td>
</tr>
<tr>
<td>Vempati 2009</td>
<td>2 months</td>
<td>1.5 hours, daily</td>
<td>Yoga</td>
<td>0.013 57</td>
</tr>
</tbody>
</table>

D. Pacheco, J of Asthma, 2012
Summary:

Patients can improve their asthma by:

• 1. Using maintenance medications regularly can decrease EIB

• 2. Pre-medicating before exercise with albuterol can eliminate EIB in some

• 3. Warming up, hydrating and cooling down is important to decrease EIB

• 4. Exercising regularly can improve quality of life, improve asthma control and reduce T-helper cell induced inflammation
Please contact me at

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Have a great day