TOP PERFORMANCE OF ATHLETES WITH ASTHMA

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I have no financial relationships to disclose.

I will not discuss off label use and/or investigational use in my presentation.
LEARNING OBJECTIVES

- Understanding definition and pathophysiology of asthma and exercise induced bronchospasm.
- Describe testing to confirm asthma diagnosis.
- Describe treatment and best management of asthma in athletes
DEFINITION OF ASTHMA

- A chronic inflammatory disorder of the airways in which many cellular mechanisms are involved.
- Chronic inflammation in the airways leads to airway hyper-responsiveness.
- Airway hyper-responsiveness leads to symptoms of cough, wheeze and shortness of breath.
- Recurrent symptoms lead to airflow obstruction that resolves either spontaneously or with treatment.
DEFINITION OF EXERCISE INDUCED BRONCHOSPASM

- Airway narrowing that occurs as a result of exercise.

Pathophysiology of EIB

- 2 theories: Thermal hypothesis and osmotic hypothesis
  - Thermal hypothesis: airway cooling during exercise causes vasoconstriction and subsequent rewarming after exercise causes hyperemia and edema.
  - Osmotic hypothesis: due to high minute ventilation water is lost from airway leading to increase in osmolarity of airway surface which leads to dehydration of epithelial cells which causes an inflammatory response making smooth muscle contraction and edema.
EXERCISE INDUCED ASTHMA VS EXERCISE INDUCED BRONCHOSPASM….

- Occurs in both asthmatics and non asthmatics
- Prevalence unknown but estimates 20% in non asthmatics and 30-70% in top performing athletes.
- Some controversy exists whether bronchospasm induced only by exercise should be called asthma
- Most feel that EIB is not an isolated phenomenon but a reflection of underlying asthma.

Jackie Joyner-Kersee: all time greatest female athlete in heptathlon and long jump, 3 gold, 1 silver, 2 bronze Olympic medals.

Diagnosed with asthma age 18.
WHAT PERCENTAGE OF OLYMPIC ATHLETES HAVE ASTHMA?

- A. 5-10%
- B. 15-20%
- C. 40-50%
- D. none of the above
WHAT PERCENTAGE OF OLYMPIC ATHLETES HAVE ASTHMA?

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ASTHMA IN THE ELITE ATHLETES

- Prevalence of asthma and EIB are increased in elite athlete
  - 8% of Olympic Athletes have asthma.
  - 17% of Olympic long distance runners
  - 80% of competitive cross-country skiers from Norway and Sweden
  - 55% of competitive figure skaters
  - 35% of elite ice hockey players
  - 76% elite swimmers

The Physician and Sportsmedicine Sept 2011, 39 (3); 163-170
DOES ENDURANCE TRAINING PROMOTE THE DEVELOPMENT OF ASTHMA?

- Mechanical stress of extreme breathing on airway epithelial cells may release inflammatory mediators leading to airway remodeling
- Age of onset is unusually high in endurance winter athletes
- Role of long term intense endurance training
Ice rink athletes: inhalation of cold dry air in combination with emissions from resurfacing machines

Nordic skiers: high minute ventilation of cold dry air

Swimmers: high levels of trichloramines in pool air

Long distance runners: high minute ventilation and exposure to outdoor allergens and ozone
DIAGNOSIS OF ASTHMA IN ELITE ATHLETE

- Symptoms: shortness of breath, chest tightness, chest pains, chest pressure
- Exam: generally normal
- Objective testing
  - Bronchial provocation tests
  - peak flow before and after exercise not accurate
Exercise challenge test: 6-10 min of ergometer or treadmill exercise.
- test positive if FEV1 falls by 10%
- Exercise testing in lab has low yield and poor reproducibility

Eucapnic voluntary hyperpnea test
- Subject breaths dry air containing 5% CO2 for 6 min through low resistance circuit at a high rate
- Positive test >10% reduction in FEV1

Hyperosmolar (4.5%) saline test: FEV1 decrease by 15%

Inhaled Mannitol testing: FEV1 decrease by 15%

Methacholine Challenge test: FEV1 decrease by 20%
TYPICAL APPEARANCE OF ASTHMA BY SPIROMETRY

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post BD</th>
<th>% CHAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
<td>5.22</td>
<td>5.88</td>
<td>103%</td>
</tr>
<tr>
<td>FEV1</td>
<td>3.73</td>
<td>4.71</td>
<td>99%</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>71%</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>FEFmax</td>
<td>8.80</td>
<td>10.45</td>
<td>120%</td>
</tr>
<tr>
<td>FEF(25-75)</td>
<td>1.74</td>
<td>4.18</td>
<td>83%</td>
</tr>
</tbody>
</table>

After Albuterol BD.
CLASSIFICATION OF ASTHMA BY SPIROMETRY

- Severity of airflow obstruction by predicted FEV1
  - Normal 80-100%
  - Mild airflow obstruction >80%
  - Moderate airflow obstruction 60-80%
  - Severe airflow obstruction <60%
- Reversible airflow obstruction
- ATS guidelines after administration of bronchodilator
  - FEV1 > 200mL and
  - Change in FEV1 > 12%
Paula Radcliffe fastest female marathon in world 2hr 15 min 25 sec

Diagnosed with asthma age 14.
DIFFERENTIAL DIAGNOSIS IN ASTHMA

- Cardiac disease
  - ASD, VSD, valvular disease
  - SVT
- Exercise-induced laryngeal dysfunction
  - Vocal cord dysfunction
  - Laryngomalacia
  - Exercise induced laryngeal prolapse
- Mechanical airway obstruction
  - Tumor, foreign body
- Hyperventilation
- Normal physiological exercise limitation
  - Most difficult to hear and often the biggest work up
NATIONAL ASTHMA EDUCATION AND PREVENTION PROGRAM 2007 AND EXPERT PANEL REPORT 2009

http://www.nhlbi.nih.gov/guidelines/asthma/
TREATMENT OPTIONS

- Exercise induced bronchospasm only
  - Warm up before exercise
  - PRN short acting $\beta_2$-agonist (albuterol) 10-15 minutes before exercise. Should last 2-4 hours
  - Leukotriene receptor antagonist
  - Inhaled Cromolyn sodium
  - ATS consensus statement recommends against long acting $\beta_2$-agonist

- Exercise induced bronchospasm in the asthmatic
  - Treat underlying asthma per guidelines
  - PRN use of short acting $\beta_2$-agonist
Amy van Dyken: 6 Olympic gold medals

Diagnosed with asthma age 6
B₂-AGONIST FOR EXERCISE-INDUCED ASTHMA

- Cochrane Database: 53 randomized, double blind, placebo controlled trials consisting of 1139 participants.

- Primary outcomes for short-term administration, data on maximum fall in FEV₁ showed a significant protective effect for both short-acting beta-agonists and long-acting beta-agonists compared with placebo, with a mean difference of -17.67% (95% confidence interval (CI) -19.51% to -15.84%, P = 0.00001.

- Long-term use of both short acting β₂-agonist and long acting β₂-agonist induced the onset of tolerance and decreased the duration of drug effect even after a short treatment period.
## Classifying Asthma Severity in Youths $\geq 12$ Years of Age and Adults

### Components of Severity

<table>
<thead>
<tr>
<th>Impairment</th>
<th>Intermittent</th>
<th>Persistent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal FEV$_1$/FVC:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-19 yr</td>
<td>$85%$</td>
<td>Mild</td>
</tr>
<tr>
<td>20-39 yr</td>
<td>$80%$</td>
<td></td>
</tr>
<tr>
<td>40-59 yr</td>
<td>$75%$</td>
<td></td>
</tr>
<tr>
<td>60-80 yr</td>
<td>$70%$</td>
<td></td>
</tr>
<tr>
<td>Symptoms</td>
<td>$\leq 2$ days/week</td>
<td>$&gt;2$ days/week but not daily</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>$\leq 2x/month$</td>
<td>3-4x/month</td>
</tr>
<tr>
<td>Short-acting beta$_2$-agonist use for symptom control (not prevention of EIB)</td>
<td>$\leq 2$ days/week</td>
<td>$&gt;2$ days/week but not daily, and not more than 1x on any day</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
<td>Minor limitation</td>
</tr>
<tr>
<td>Lung function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Normal FEV$_1$ between exacerbations</td>
<td>• FEV$_1$ $&gt;80%$ predicted</td>
<td>• FEV$_1$ $&gt;60%$ but $&lt;80%$ predicted</td>
</tr>
<tr>
<td>• FEV$_1$/FVC normal</td>
<td>• FEV$_1$/FVC normal</td>
<td>• FEV$_1$/FVC reduced 5%</td>
</tr>
</tbody>
</table>

### Risk

- Exacerbations requiring oral systemic corticosteroids
  - 0-1/year (see note)
  - $\geq 2$/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

<table>
<thead>
<tr>
<th>Step</th>
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<tbody>
<tr>
<td>Step 1</td>
<td></td>
</tr>
<tr>
<td>Step 2</td>
<td></td>
</tr>
<tr>
<td>Step 3</td>
<td>and consider short course of oral systemic corticosteroids</td>
</tr>
<tr>
<td>Step 4 or 5</td>
<td></td>
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</tbody>
</table>

**Key:** FEV$_1$, forced expiratory volume in 1 second; FVC, forced vital capacity; ICU, intensive care unit.

**Note:** At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma severity. In general, more frequent and intense exacerbations (e.g. requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate greater underlying disease severity. For treatment purposes, patients who had $\geq 2$ exacerbations requiring oral systemic corticosteroids in the past year may be considered the same as patients who have persistent asthma, even in the absence of impairment levels consistent with persistent asthma.
TREATMENT OF ASTHMA

- GINA (Global Initiative for Asthma) guidelines
- NHILB guidelines
- Symptoms 2x per week
  - $\beta_2$-agonist
- Symptoms >2x per week
  - Leukotriene receptor antagonist daily or inhaled corticosteroid
  - Rescue $\beta_2$-agonist
- Next step
  - Inhaled corticosteroid plus leukotriene receptor antagonist or long acting $\beta_2$-agonist
- Next step
  - Follow the guidelines
STEPWISE APPROACH FOR MANAGING ASTHMA AGED ≥12 YEARS

Step 1
Preferred: SABA prn

Step 2
Preferred: Low-Dose ICS (A)
Alternative: Cromolyn (B), Nedocromil (B), LTRA (B), or Theophylline (B)

Step 3
Preferred: Medium-Dose ICS (A)
or
Low-Dose ICS + LABA (A)
Alternative: Medium-Dose ICS and either LTRA (B), Theophylline (B), or Zileuton (D)

Step 4
Preferred: High-Dose ICS + LABA (B)
Alternative: High-Dose ICS and either LTRA (B), Theophylline (B), or Zileuton (D)

Step 5
Preferred: Oral Corticosteroid

Step 6
Preferred: Omalizumab for Patients Who Have Allergies (B)
Jerome Bettis: played 13 seasons with NFL

Diagnosed with asthma age 14
DO INHALED $B_2$-AGONIST IMPROVE PERFORMANCE IN NON-ASTHMATIC ATHLETES?

- A. Yes
- B. No
- C. I don’t know.
DO INHALED $\mathrm{B}_2$-AGONIST IMPROVE PERFORMANCE IN NON-ASTHMATIC ATHLETES?

- A. Yes
- B. No
- C. I don’t know.
DO INHALED $\beta_2$-AGONIST HAVE AN ERGOGENIC POTENTIAL IN NON-ASTHMATIC COMPETITIVE ATHLETES?

- 17 of 19 randomized placebo-controlled trials in non-asthmatic competitive athletes no performance enhancement was found with the use of $\beta_2$-agonist (formoterol, salbutamol, salmeterol and terbutaline)
- This was particularly true for endurance performance, anaerobic power and strength performance.
- In 3 of 4 studies supratherapeutic doses of salbutamol had no ergogenic effect

Kindermann, Sports Medicine 2007
INFLUENCE OF A B₂-AGONIST ON PHYSICAL PERFORMANCE AT LOW TEMPERATURE IN ELITE ATHLETES

- 20 elite male athletes, no history of allergy or airway disease, normal spirometry and methacholine challenge tests performed a maximal exercise test on a treadmill in a climate chamber at 10 degrees C on two subsequent days.

- Before exercise they inhaled terbutaline (3 mg from MDI) or placebo in a randomized, single blind manner. After 10-min warm-up on the treadmill, a submaximal work preceded a stepwise increase of the workload until exhaustion. Lung function, ventilation, oxygen uptake, and heart rate were determined.

- Terbutaline induced a significant bronchodilatation; FEV₁ increased from 4.8 (4.4-5.1) L to 5.0 (4.6-5.4) L, mean (95% CI).

- There were no significant differences between the two treatments with regard to exercise time, 25.1 (24.3-25.8) min vs 24.9 (24.1-25.6) min, oxygen uptake and ventilation during exercise, or heart rate at maximal workload.

INHALED B₂-AGONIST AND PERFORMANCE IN COMPETITIVE ATHLETES

- 20 randomized placebo controlled trials on β₂-agonist in non-asthmatic competitive athletes demonstrated no ergogenic benefit to use of β₂-agonist.
- 3 studies frequently cited that do demonstrate ergogenic effects were not robust studies and have been criticized overall as not indicative of effects in high performance athletes.
- β₂-agonist are banned by IOC and WADA and asthmatics must prove medical need to get exemption.
Objective testing required to confirm diagnosis

- Spirometry with FEV1
- If normal FEV1 then bronchial provocation test is required
- If airflow obstruction present then inhalation of bronchodilator done to test for reversibility.

Treatment

- Follow GINA guidelines (Global Initiative for Asthma)
- Reduce exposures
- Warm-up may help
- ICS and some inhaled β2-agonist okay with Therapeutic Use Exemption Standard
- All systemic β2-agonist are prohibited
- All systemic corticosteroids are prohibited
INTERNATIONAL OLYMPIC COMMITTEE CHANGES AS OF 2010

- Albuterol (salbutamol), salmeterol and formoterol okay and no longer requires a therapeutic use exemption.
- Maximum dose of albuterol 1600 ug/24 by inhalation. If found in urine in excess of 1000 ug/ml then athlete’s use of drug is called into question.
- Oral or injected β₂-agonist prohibited.
- Inhaled corticosteroids permitted.
- Oral or injected steroids prohibited.
- Leukotriene receptor antagonists permitted.
Dennis Rodman: won 5 NBA championships and is felt to be the best rebounding forward in NBA history.

Known Internationally for his fame in North Korea.

Diagnosed with asthma
PEARLS

- Asthma is extremely common in elite athletes
- Inhaled $\beta_2$-agonist do not enhance performance in elite athletes without asthma.
- Management of asthma in elite athletes should follow national guidelines.
END
REFERENCES

REFERENCES

- Cochrane Database systematic review: $\beta_2$-agonist for exercise induced asthma. October 2013.