

Exercise-Induced Bronchoconstriction (EIB)
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No disclosures

Objectives

- What is Exercise-Induced Bronchoconstriction?
- Pathogenesis
- Role of the Environment
- Establishing the Diagnosis
- Pharmacologic Treatment
- Non-pharmacologic Therapy
- Screening for EIB
- Exercise, Asthma & Doping

EIB: Description

- Acute airway narrowing that occurs as a result of exercise
- Exact prevalence of EIB in patients with asthma is **not** known
- Common triggers of bronchoconstriction in patients **with** asthma.
- It may also occur in up to **20%** of individuals **without** asthma
- Nomenclature controversy: **EIB vs. EIA**

EIB: Clinical Presentation

- Variable & Non-Specific Symptoms
- Presence or Absence of Specific Respiratory Symptoms:
Poor Predictive Value for EIB
- Chest Tightness, Cough, Wheezing & Dyspnea
- Provoked by Exercise or may only occur in Specific Environments: Ice rinks or Indoor pools
- Often Mild to Moderate in Severity (Severe episodes of EIB may occur)

Etiology of EIA: 2 Theories

- **Hyperosmolar Theory**
 - Water loss from airway surface liquid → Hypertonicity → Release of pro-inflammatory mediators
 - Inhalation of Hyperosmolar saline → EIB
 - Why/how this stimulates mediator release is **not** known?
- **Airway Re-Warming Theory**
 - Exercise-induced Hyperventilation → Heat transfer from Pulmonary Vascular Bed & Cooling of Airway Surface. After Exercise: Re-warming & Bronchiolar Vasodilation, Fluid Exudation, Mediator Release & Bronchoconstriction

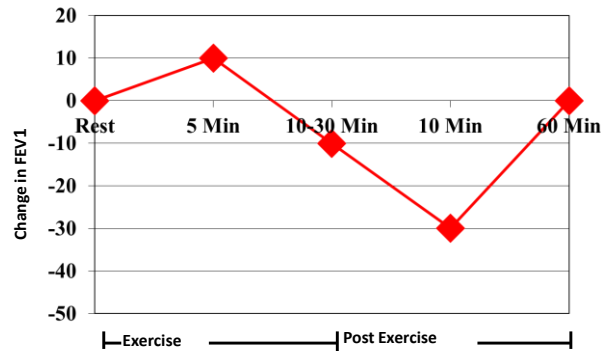
Role of The Environment

- **≈ 30% prevalence of EIB in Ice rink athletes** (inhalation of cold, dry air & pollutants from fossil-fueled resurfacing machines)
- **Skiers** (high ventilation inhalation of cold, dry air)
- **Up to 30% of asthma & EIB in swimmers** (high levels of trichloramines in indoor pool air)
- **High prevalence among distance runners** (high allergen & high ozone environments)
- **Environmental exposures:** cold air, dry air, ambient ozone & airborne particulate matter
- **Susceptible populations** i.e.: children with pre-existing CV disease, diabetes, or lung disease, more sensitive to particles in the lungs during exercise

Establishing the Diagnosis

- Established by changes in lung function post exercise, **NOT** on the basis of symptoms
- Symptoms: cough, shortness of breath, wheeze & mucus production neither sensitive, nor specific for EIB
- EIB may be identified in those without symptoms & many individuals with respiratory symptoms will not have EIB

Time Course of EIB



Measuring & Quantifying EIB

- Serial lung function measurements after exercise or hyperpnea to determine if EIB is present.
- FEV₁ preferred (better repeatability & more discriminating than peak expiratory flow rate)
- Severity may be graded mild, moderate, or severe
- Recovery from EIB usually spontaneous. FEV1 returns to 95% baseline value within 30 – 90 min.

Exercise Challenge Testing to Identify EIB

- Determinants of Airway Response to Exercise: Type, Duration & Intensity of Exercise & Temperature & Water Content of the Air Inspired
- Time since Last Exercise (some individuals refractory to another exercise stimulus up to 4 hours)
- Most Important Determinants of EIB: Sustained High Level of Ventilation & Water Content of Air Inspired

Simple Exercise Challenge Protocol

- Baseline spirometry to determine FEV₁
- Rapid increase in exercise intensity over 2 – 4 min
- Breathe dry air (<10mg H₂O/L) with a nose clip in place while exercising
- Load to raise heart rate (HR) to 80% of max predicted (predicted max HR ≈ 220 - age in years)
- Sustained exercise for 4-6 minutes at that HR
- Running > cycling to achieve targets
- Repeat spirometry immediately post exercise and at 5, 10, 15 & 30 minutes post exercise & 15 min post bronchodilator
- Positive test: ≥10% fall in FEV₁ (some labs ≥ 15%)

What to Avoid Before Testing?

- Short acting & long-term preventive asthma meds
- Recent Intense or Intermittent warm-up exercise
- Recent use of non-steroidal anti-inflammatory meds
- Recent exposure to inhaled allergens
- Anti-histaminics

Surrogates for Exercise Testing

- Eucapnic Voluntary Hyperventilation with dry air
- Inhalation of 4.5% Hypertonic Saline
- Inhalation of Dry Powder Mannitol
- Sport-specific Exercise for Athletes
- Methacholine Challenge (MCH) Test

Treatment:

Pharmacologic & Non-Pharmacologic

- Pharmacologic
 - Short-acting Beta agonists (SABAs)
 - Long-acting Beta agonists (LABAs)
 - Leukotriene Receptors Antagonists (LTRAs)
 - Inhaled Corticosteroids (ICS)
 - Cromolyn/Nedocromil (No longer available in USA)
 - Anticholinergic (minor role)

Treatment

- **Non Pharmacologic**
 - Warm up to induce a refractory period
 - Maneuvers to pre-warm & humidify air during exercise (breathing through mask or scarf)
 - Improving general physical conditioning
 - Losing weight if obese

1. Should patient with EIB be treated with an Inhaled SABA before exercise?

- Use of short-acting bronchodilators(β_2 -agonists)i.e.: albuterol *PRN*
- Stimulate β_2 receptors on airway smooth muscle \rightarrow muscle relaxation & bronchodilation. May prevent mast cell degranulation
- Inhalation 15 – 20 min before exercise
- Effective for 2 – 4hrs in preventing or attenuating EIB
- May fail to prevent EIB in 15-20% patients with asthma

Treatment

continued

- Daily use of β_2 -agonists alone or combined with ICS \rightarrow **Tolerance** (\downarrow duration of protection & \uparrow recovery in response to SABA after exercise)
- Tolerance may be due to desensitization of β_2 receptors on airway smooth muscle & mast cells
- Use of SABA should be < daily
- A controller agent (ICS or LTRA) is generally ADDED whenever SABA is used daily

#2. Should patients with EIB be treated with an Inhaled LABA?

- LABAs: effective in treating & preventing EIB (6-12 hrs)
- Protective effect decreases with daily use to 6 hrs. after daily use for 30 days
- Concomitant use of ICS does not mitigate this loss of effectiveness
- Concerns RE: increased morbidity & mortality with use of LABAs as monotherapy
- Risks > Benefits

3. Should patients with EIB be treated with ICS?

- Daily ICS **most** effective anti-inflammatories for EIB
- Effect may be due to better control of asthma & direct therapeutic effect on airway inflammation in EIB
- ICS may be used alone or in combination
- ICS does **NOT** prevent tolerance from daily β_2 -agonist
- It may take up to 4 weeks after initiation of therapy for maximum benefit against EIB & is dose dependent
- Patients with EIB who continue to have symptoms despite using an inhaled SABA before exercise, or who require an inhaled SABA daily or more frequently: Daily Administration of ICS

Treatment

continued

- Patients with EIB who continue to have symptoms despite using an inhaled SABA before exercise, or who require an inhaled SABA daily or more frequently: **Daily Administration of ICS**
- Daily administration of LTRA
- Add daily ICS vs. daily LTRA to prn SABA in patients with EIB: personal preference!

4. Should patients with EIB be treated with LTRAs?

- ▶ LTRAs (montelukast) once daily will reduce EIB & improve recovery to baseline
- ▶ Effect < ICS or pre-exercise SABA
- ▶ Duration of action lasts up to 24 hours!
- ▶ LTRAs should be taken < 2 hours before exercise for maximal effect for those **not** exercising daily
- ▶ LTRAs appear to protect against EIB in asthma or elite athletes without asthma

5. Should patients with EIB be treated with an antihistamine?

- Patients with **EIB and Allergies**, who continue to have symptoms despite using an inhaled SABA before exercise, or who require an inhaled SABA daily or more frequently, it is suggested to consider using an antihistaminic
- For nonallergic patients with EIB (as above), antihistaminic is not recommended

6. Should patients with EIB be treated with a short-acting anticholinergic?

- For patients with EIB who continue to have symptoms despite using an inhaled SABA before exercise, or who require an inhaled SABA daily or more frequently, an anti-cholinergic may be considered

7. Should patients with EIB engage in a physical activity before exercise, to induce a refractory period?

- 10-15 minutes warm up before exercise or competition, reduces EIB for next 2 hrs. "refractory period"
- Interval or combination warm up recommended
- Physical conditioning may alleviate EIB (lower minute ventilation required for any given workload once CV condition is improved)

Why is exercise good for people with asthma?

- Increases aerobic capacity
 - Greater activity for less ventilation
- Improves cardiovascular fitness
- Improves symptom control
- Enhances self-confidence

Asthmogenic Activities

- Continuous hard exercise
- Exercise in cold environment
- Exercise in polluted air, either indoor (skating rink) or outdoor
- Exercise during pollen season for allergic athletes
- Exercise during an upper or lower respiratory infection

High Asthmogenic Activities

- Long-distance running
- Cycling
- Soccer
- Rugby
- Basketball
- Ice hockey
- Ice skating
- Cross country skiing

Less Asthmogenic Activities

- Intermittent exercise or team games
- Swimming
- Exercise in warm, humid air
- Exercise outside of the pollen season or in non-polluted air

Low Asthmogenic Activities

- | | |
|-------------------|---------------|
| ■ Tennis | ■ Sprinting |
| ■ Gymnastics | ■ Handball |
| ■ Golf | ■ Football |
| ■ Karate | ■ Baseball |
| ■ Wrestling | ■ Diving |
| ■ Boxing | ■ Racquetball |
| ■ Downhill skiing | ■ Isometrics |
| ■ Water polo | |

Swimming and Asthma

- High humidity is a partial explanation
- Prone position
 - Alters ventilation/perfusion distribution
- Slow exhalation and rhythmic breathing
 - Lower ventilation with lower RR despite increased TV
 - ↑CO₂ → bronchodilation and ↑bronchial blood flow
- Immersion in water
 - Improved gas exchange & ventilatory efficiency
- Chlorine in water may exacerbate symptoms

Skiers/Ice Hockey and Asthma

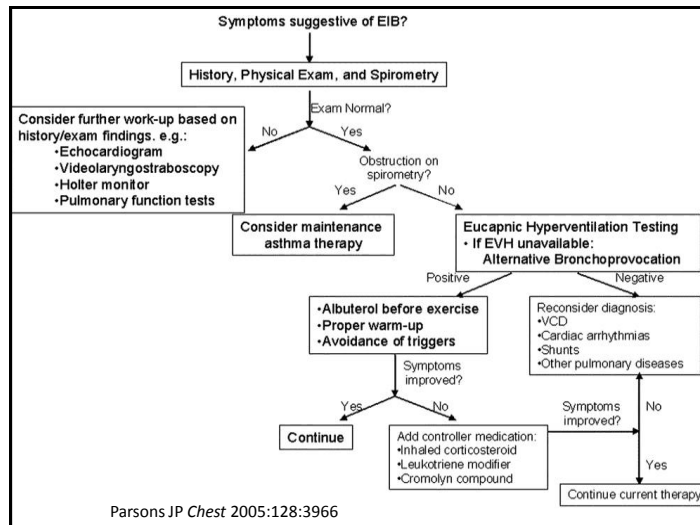
- High prevalence of asthma
- Inflammatory infiltrate (by biopsy) has neutrophils, fewer eosinophils, mast cells & macrophages compared to individuals with asthma
- Extreme cold may damage the airway epithelium directly

EIB and Asthma

- EIB one of the first symptoms of asthma to emerge and the last to resolve after treatment with an ICS
- EIB correlates with the number of asthma attacks per year
- ICS before exercise will **not** relieve EIB
- ICS will attenuate EIB by ~50%

Exercise, Asthma & Doping

- **Doping:** Use of any banned substance (including drugs & blood products) to improve athletic performance
- All B₂ agonists are banned in competition except inhaled albuterol (1600ucg/24h) and LABAs salmeterol & formoterol (54ucg/24h)
- These same medications would **not** be allowed in athletes who do not have asthma
- IOC: "There is no scientific evidence to confirm that inhaled B₂ agonists enhance performance in doses required to inhibit EIB".
- Oral or injected B₂ agonists are banned.
- Steroids are prohibited if given oral, IV or IM



Why Do We Miss the Diagnosis?

- **Some children with asthma do not perform exercise of a sufficient magnitude**
 - How much exercise do you perform?
 - What is your exercise tolerance?
 - What symptoms do you have after exertion?
- **Symptoms can be vague**
 - "I must be out of shape"
 - Stomach or muscle cramps
 - Headache
 - Generalized fatigue
 - Chest discomfort
 - "Everyone else coughs-it is normal"
 - Chest pain

Failure to Respond: Look Elsewhere Differential Diagnosis

- Deconditioning
- Vocal cord dysfunction
- Cardiac disease
- Central airway obstruction
- Pulmonary disorders
- Muscle disorders

Take Home Message

- EIB frequently goes undiagnosed
- EIB is undiagnosed in children with asthma if you use symptoms only
- EIB is undiagnosed in athletes even in elite athletes
- EIB is especially common in elite athletes in winter sports

In Summary

- EIB is under-diagnosed and may be difficult to diagnose
- EIB can exist in the absence of asthma
- Some activities are more asthrogenic than others
- SABAs are effective most of the time for most children
- A warm up and cool down period may help to reduce symptoms

Vocal Cord Dysfunction

- Often associated with inspiratory stridor after exercise
- Typical finding: abnormal adduction of the vocal cords on inspiration
- Direct visualization of the vocal cords with rhinolaryngoscopy preferably during exercise

More on Vocal Cord Dysfunction

- ▶ Typical presentation: young female athlete with over-achieving personality traits and perceived psychosocial stresses
- ▶ It is common in athletes: ~5%
- ▶ Co-exists with EIB in 50-55% of individuals
- ▶ Pearl to diagnosis: Localize their symptoms to the throat and not the chest
- ▶ Treatment: Behavioral therapy
 - ▶ Tightening/relaxing exercises, diaphragmatic breathing

Reference:

**Journal of Allergy and Clinical
Immunology, Volume 13, Issue
5, November 2016**

**Practice parameter: Exercise
induced bronchospasm**