Practical Approaches to
the Recognition and
Management of Asthma-
induced Effects on
Exercise Tolerance

An interactive workshop led by:
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Disclosures
1. Dr. Gregory has no financial conflicts to disclose.
2. Dr. Bowman is retired from the Med Univ S Carolina; he is on the speakers bureau for Monaghan and a consultant for Thermo-Fisher. Neither will influence his presentation.
3. In the presentation, both speakers will only speak about medications in accord with their licensure.
4. It is important for members of the audience to recognize the relative chaos of licensure of asthma medications in children.

Educational Objectives
Members of the audience will be able to:
1. Describe innovative ways to utilize school personnel to improve overall management and control;
2. Outline the importance of including good exercise tolerance as a marker of excellent asthma control;
3. Describe how exercise intolerance may or may not reflect poorly – controlled asthma;
4. Identify ways they plan to use exercise tolerance as a marker of severity and control of asthma in their own practice / work setting.
Challenges with Exercise for Children with Asthma – Practical Approaches

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Exercise-Induced Bronchoconstriction (EIB)

Transient and reversible acute airway narrowing that occurs during or after exercise in the presence or absence of clinically recognized asthma 1,2,3

Clinical Pearl:
- The term exercise-induced asthma (EIA) is not used as it may imply incorrectly that exercise causes rather than exacerbates or triggers asthma symptoms 4.

Prevalence of EIB in Children

- General population approximately 5–20%1
- Approximately 40% to 60% of individuals with asthma have EIB2,3
- Affects up to 80% of children with asthma4
- Prevalence is greater in high-performance athletes than in the general population owing to prolonged inhalation of cold, dry air, aeroallergens and airborne pollutants5.

EIB: The Facts

- Exercise is one of the most common triggers of bronchoconstriction.
- EIB can occur without a diagnosis of asthma.
- EIB is frequently documented with asthma and reflects insufficient control of underlying asthma.
- Exercise-induced respiratory symptoms have a poor predictive value for airway hyperreactivity.

Pathobiology

- During exercise-related hyperventilation, transient osmotic change at the airway surface occurs causing reduction in epithelium liquid volume.
- Hypovascular environment leads to:
  - Mast cell degranulation
  - Airway smooth muscle contraction
  - Increased mucus production
  - Microvascular permeability
  - Sensory nerve activation
  - Bronchoconstriction
  - Airway edema

Role of Mast Cells, Eosinophils and Mediators

- Mast cells and eosinophils appear to play a major role in the pathogenesis of EIB.
- Peripheral blood eosinophil counts are associated with severity of EIB.
- Patients with asthma and EIB are more likely to have a greater concentration of eosinophils in sputum than those without EIB.
**EIB: Osmotic vs Thermal Theory**

Hyperventilation through the mouth associated with intense exercise causes the need for humidifying and heating large volumes of air during a short period of time.

**Osmotic theory**
- Mucosal dehydration
- Increased osmolarity
- Cell volume changes
- Mediators released
- Smooth muscle contraction
- Vascular leakage
- Edema

**Thermal theory**
- Mucosal cooling
- Vasoconstriction
- Rapid re-warming of the airway
  - Reaction hyperemia
  - Vascular engorgement
- Vascular leakage & edema

Exercise-induced Bronchoconstriction

**Clinical Symptoms of EIB in Children**

**Most Common**
- Wheeze
- Chest tightness
- Dyspnea
- Cough
- Chest pain (primarily in children)
- Excessive mucus production

**Non-specific**
- Chest pain
- Poor exercise performance
- Avoidance of activity
- Difficulty keeping up with peers

**Impact of EIB in Pediatric Asthma**

Physical activity is fundamental for growth and long-term development in children!

- Associated with physical and emotional burden
- Significantly reduces participation in physical activity/sports
- Negative association with QoL regardless of the severity of asthma symptoms
- Stop exercising because of EIB symptoms

Children may experience
- Fear
- Bullying
- Social isolation
- Depression
- Anxiety
- Poor health
- Obesity

- Generally occur during or within 5 to 30 minutes after intense exercise
Which Sport is Best for Children with EIB?

Sports and activities most likely to cause EIB symptoms are those requiring constant activity or performed in cold weather.

Low-risk:
- short duration
- high ventilatory levels are not reached

Medium-risk:
- alternation of aerobic and anaerobic phases
- brief periods of continuous high-intensity exercise (5–8 min)

High-risk:
- endurance and winter sports
- physical effort high ventilatory levels are reached


Sports and Potential Risks of EIB

<table>
<thead>
<tr>
<th>Low-risk sports</th>
<th>Medium-risk sports</th>
<th>High-risk sports</th>
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<tbody>
<tr>
<td><em>&lt;5 minutes effort</em></td>
<td><em>Continues effort no more than 5–8 minutes</em></td>
<td><em>&gt;5–8 minute effort and/or in cold/dry environment</em></td>
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- Track and field
  - sprint
  - hurdle
  - jump
- Soccer
- Tennis
- Rugby
- Fencing
- American football
- Gymnastics
- Basketball
- Cross-country skiing
- Downhill skiing
- Baseball
- Hockey
- Boxing
- Field hockey
- Ice hockey
- Golf
- Swimming
- Weightlifting
- Martial arts

Studies do not show consistent effect of swimming, asthma risk and EIB

- Swimming has been considered safe and recommended for patients with asthma.

- Conflicting data:
  - increased risk of EIB
  - Competitive swimmers show a high prevalence of asthma and EIB

Possible rationale:
- Increased risk of EIB with swimming and pool attendance
- Association shown between chlorinated pools and prevalence of childhood asthma
- Chlorine has strong oxidizing potential and has been shown to cause epithelial damage

Medical treatment regimen and physical activities must be adapted to each situation.

The most important thing is to choose a sport the child enjoys!

Management of EIB

- Prevent and treat bronchoconstriction
- Non-Pharmacological Management
- Patient education

Management of EIB is based on the understanding that EIB susceptibility varies widely among patients with asthma and in the absence of asthma.

Management of EIB: 
Treat Bronchoconstriction

- Management of EIB protocols are well established.
- Short-acting β-agonist (SABA) bronchodilators treatment of choice.
  - Inhaled SABAs should only be used in response to an EIB episode or up to 2-4 times per week ahead of exercise likely to induce EIB.
  - Daily use of SABAs can quickly result in tolerance and limit its effectiveness.
- Leukotriene receptor antagonists should be considered.
- Uncontrolled EIB requires further evaluation by an asthma specialist.
- Guideline-based use of combination therapy.
- Poor response to therapy.
  - Poor adherence, improper inhaler technique and exposure to environmental triggers.

Management of EIB: 
Non-Pharmacological

- Avoid exercise in an at-risk air environment.
- Good conditioning and aerobic fitness.
  - Regular exercise prevents rapid and abrupt increased in minute ventilation which is more likely to trigger EIB.
- Gradual warm-up and cool-down periods.
- Use of face mask.
- Modifications to the activity or sport, if possible, can be helpful when the symptoms are limiting the child’s participation.

Management of EIB: 
Patient Education

- Child and parents must understand:
  - the mechanisms causing EIB
  - associated symptoms associated
  - activities that causes prolonged rapid breathing
  - treatment regimen – Asthma Action Plan
  - Correct inhaler technique
  - Identify activities that exacerbate symptoms
  - Identify therapeutic interventions
  - Adherence
  - EIB should not limit participation.
Comprehensive Asthma Action Plan

Includes:
- Management of EIB
- Daily treatment regimen
- Recognizing worsening symptoms
- Pre-medicating before sports or exercise

Current Literature Review

Periostin and EIB in Children with Asthma

- Significance of periostin as a biomarker of TH2-induced airway inflammation, and as a measure of the response to therapy.\(^1\,\text{,}\,2\)

- Periostin is induced by IL-13 and can induce proinflammatory cytokines, including thymic stromal lymphopoietin (TSLP).\(^1\,\text{,}\,2\)

- TSLP in combination with IL-33 increases mast cell formation.\(^1\)

- Prognostic relationship between periostin and risk of asthma exacerbations has been observed in clinical studies.

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86 children 6-15 years old from US, Japan and Korea
asthmatic group (n = 56) and healthy controls (n = 30)

1 Measured periostin levels in serum
1 Performed pulmonary function test: baseline measurements, post-bronchodilator inhalation tests, exercise bronchial provocation tests (BPTs), and mannitol BPTs

56 asthmatic children were divided into four groups:
asthmatics with - BPT and - mannitol BPT (n = 9)
asthmatics with + BPT but - mannitol BPT (n = 7)
asthmatics with + BPT but + mannitol BPT (n = 30)
asthmatics with - BPT but + mannitol BPT (n = 10)

Periostin levels may serve as a clinically useful biomarker for identifying EIB in asthmatic children

Periostin and EIB in Children with Asthma

• Periostin levels were significantly correlated with both the maximum decrease in %FEV₁ and mannitol PD₁₅₀ value

• Serum levels of periostin in asthmatic children with both positive exercise and mannitol BPT were significantly greater than those in asthmatic children with both negative exercise and mannitol BPT and also greater than in healthy controls

• Periostin levels may serve as a clinically useful biomarker for identifying EIB in asthmatic children

Fraction of Exhaled Nitric Oxide (FeNO) in EIB

• Schoos et al. examined the predictive value of elevated FeNO for the presence of EIB on standardized testing in 7-year-old children at risk of asthma

• FeNO and EIB were linearly associated

• FeNO cutoff of 27 parts per billion (ppb) had a specificity and a positive predictive value (PPV) of 100% for EIB

• Study supports the presence of EIB is likely in children with an elevated FeNO
Exercise-induced anaphylaxis (EIA)

anaphylaxis occurs only in association with physical exertion

Food-dependent, exercise-induced anaphylaxis (FDEIA)

- symptoms develop only if exercise takes place within a few hours of eating
- in most cases only if a specific food to which the patient is sensitized is eaten in the pre-exercise period

Anaphylaxis and Exercise

Exercise induced anaphylaxis (EIAn) is a rare and potentially fatal condition. Approximately 2–15% of all anaphylactic episodes are caused by or associated with exercise.


Food-dependent Exercise-Induced Anaphylaxis (FD-EIA)

- EIAn is more frequently occurs in atopic individuals
- Diagnoses of FD-EIAAn relies on a rigorous clinical history
- Symptoms occur from 10 minutes up to 4 hours after food allergen intake
- Generally occurs if a specific food is eaten within a few hours of exercise
- Mast cell release of vasoactive mediators during EIAn may have a role in the pathogenesis
- Gastric permeability increases during exercise, which may permit increased entry of intact or incompletely digested allergens into the circulation
- Avoid any potential trigger foods at least 4–6 hours before exercise and one hour after exercise

Summary

- EIB is described as acute airway narrowing that occurs as a result of exercise
- EIB is observed in 40 to 90% of children with asthma
- Current ATS guidelines recommends use of SABA 15 minutes before exercise
- Intensity, duration, and type of exercise is associated with occurrence of EIB with higher prevalence rates in endurance sports, winter sports, possibly swimming
- Environmental factors such as temperature of inhaled air, the humidity and intensity of exercise have a significant effect on the induction of bronchoconstriction.
- When properly managed, EIB does not restrict exercise performance

How do we generally diagnose asthma?

- “Recurrent, reactive airway disease” means it
- Happened more than once
- Was responsive to albuterol
- Airway compromise was found in some way
- Acute wheezing episode is most common
- Chronic / recurrent cough
- Recurrent and prolonged viral illnesses
- The chronic diagnosis is frequently missed.
**How can exercise tolerance help us?**

- Many kids can’t / won’t exercise
- Some say we should ask PE teachers who they view as being “lazy” to find those undiagnosed
- Must sort out conditioning vs desire vs asthma
- Many kids don’t know that others feel differently when they play, age determines how they describe what they feel.
- Exercise intolerance, obesity and asthma combine for a major challenge

**Exercise Intolerance**

- PE teachers, coaches and trainers should be attentive to the possibility of undiagnosed asthma
- Kids can’t play well when they’re sick
- Talk to the nurse, both talk to parent(s)
- Ask how the child plays at home, what they do.
- When they play, what happens?
- Has this been observed / treated in the past?

**What to do?**

- Expect normal exercise tolerance
- Observe closely what happens with exercise, what does the child / teen describe?
- Note the circumstances – effort, duration, temperature, setting, etc.
- Discuss with family; urge provider involvement
- Does albuterol (if available) help?
- Does albuterol use prevent symptoms next time?
- Does peak flow or FEV1 change with exercise (go down) and after albuterol (go up)?
How often does this happen?

- Rule of twos – symptoms twice a week or more, or two nights a month or more (not w/ exercise)
- Kids should be able to play hard every day!
- Use albuterol w/ symptoms; if better, use before
- If exercise – triggered symptoms happen often, consider use of daily controller medications;
- A child should be able to play hard every day.
- If they don’t improve (acutely or chronically), it may not be asthma.

Case Discussions -- Did you bring any?

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Case – an 8 yo boy playing basketball

1. Playing on his school team, frequently stops running and has to leave the court, usually w/ noisy breathing.
2. Another parent suggests he might have asthma and what doctor could help;
3. Primary doctor said “he’s just having frequent colds”;
4. With parental prodding, referred to pulmonologist;
5. Diagnosis of asthma made, controller / rescue started, and appropriate medication use taught;
6. Within 6 weeks, he can play hard for over an hour, never has to leave a game for breathing problems, rarely needs albuterol (with spacer).
Case – a 7 yo boy coughs in PE
1. A large 7 yo boy lags behind classmates in PE and sits during recess;
2. The PE teacher notices that he often coughs when active and always finishes in the last 3 if running;
3. She talks to the nurse who notes that he misses a lot of school, frequently more than a week at a time;
4. RN talks to mom who then talks to the pediatrician;
5. They try albuterol with exercise; that helps some;
6. Since he still takes albuterol 4 – 5 times per week, they start a controller (with rescue as needed);
7. His exercise tolerance markedly improves;
8. He needs albuterol about twice a month.

17 yo teen who can’t exercise
In the past, he was a competitive soccer player but now can’t do any PE or sports;
1. Chief complaint – “I can’t breathe” (very common)
2. Pulmonary function tests show mild airway responsiveness to albuterol (FEV1 up 12%);
3. Controllers and frequent albuterol didn’t really help;
4. Multiple alternative diagnoses considered;
5. Further questioning – “I feel like I’m breathing through a straw” and points to larynx;
6. Ultimately found to have paradoxical vocal cord movement, with VC spasm on exercise test.

Can’t get through football practice
1. 15 yo boy with asthma can’t get through summer football practice in spite of regular controller use;
2. Last year he did well playing on the JV squad;
3. Now, he starts out well, but after 20 – 30’ he gets SOB and needs albuterol rescue, every evening of practice;
4. Albuterol pre-practice helps slightly, but he still needs rescue 1 – 3 more times each evening, especially with conditioning runs after practice;
5. His controller is changed to a combo medication with some improvement, but still needs daily rescue;
6. Evening controller dose was moved to 5:30;
7. Much improved, no longer needing rescue.
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QUESTIONS?