

Exercise-Induced Asthma (EIA)

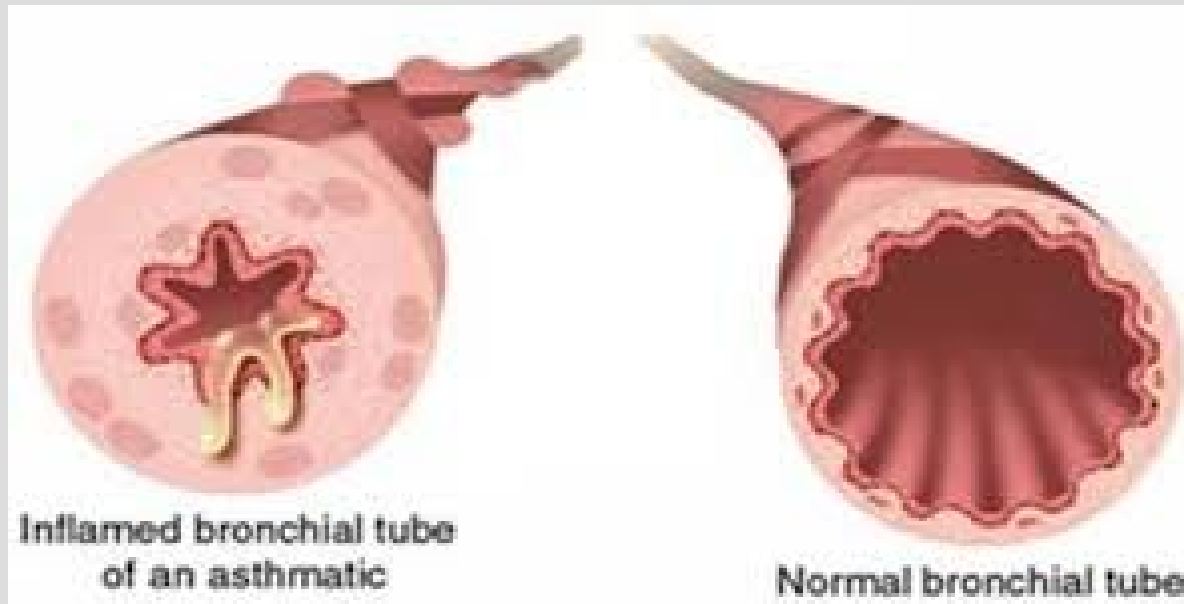
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Exercise-Induced Asthma

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**Exercise-induced asthma occurs when
the airways narrow as a result of
exercise**



- Doctors often call it "**exercise-induced bronchoconstriction**" instead.
- That's because exercise does not actually cause asthma.
- exercise is not an independent risk factor for asthma
- But exercise can trigger bronchoconstriction in some people who already have asthma

SO

Exercise-induced bronchoconstriction

the acute onset of bronchoconstriction
occurring during or immediately after
exercise





❖ This causes asthma symptoms about **10 to 15** minutes after starting to exercise.



❖ In most cases, the symptoms go away after about **1 hour**

❑ A person may have asthma symptoms that become worse with exercise

❑ or may have only exercise – induced bronchoconstriction, without symptoms at other times

- **These symptoms are different from shortness of breath that happens during an asthma "attack" or flare-up.**
- **A person having an asthma flare-up might have more trouble breathing if they try to exercise.**
- **That's because the airways are already narrowed**

- In fact, there is some speculation that decreased physical activity is a risk factor for asthma, and that exercise may be helpful in preventing the onset of asthma in children

EPIDEMIOLOGY

*The estimated prevalence of exercise-induced bronchoconstriction (EIB) varies from approximately **5 to 20 percent** in the general population*

up to **90 percent** of patients with
symptomatic asthma have some degree of EIB

The magnitude of EIB is most strongly correlated with the underlying degree of **airway hyperresponsiveness** and the presence of **airway inflammation** as measured by the number of airway eosinophils

Thus, many patients with mild, episodic asthma characterized by minimally increased airway responsiveness and mild airway inflammation do not experience clinically significant bronchoconstriction even with strenuous exercise.

PATHOGENESIS

1- Minute ventilation

**the volume of air inhaled or exhaled
from a person's lungs per minute
rises with exercise**



2- AIR

EIB probably results from changes in airway physiology triggered by the large volume of relatively **cool, dry air** inhaled during vigorous activity

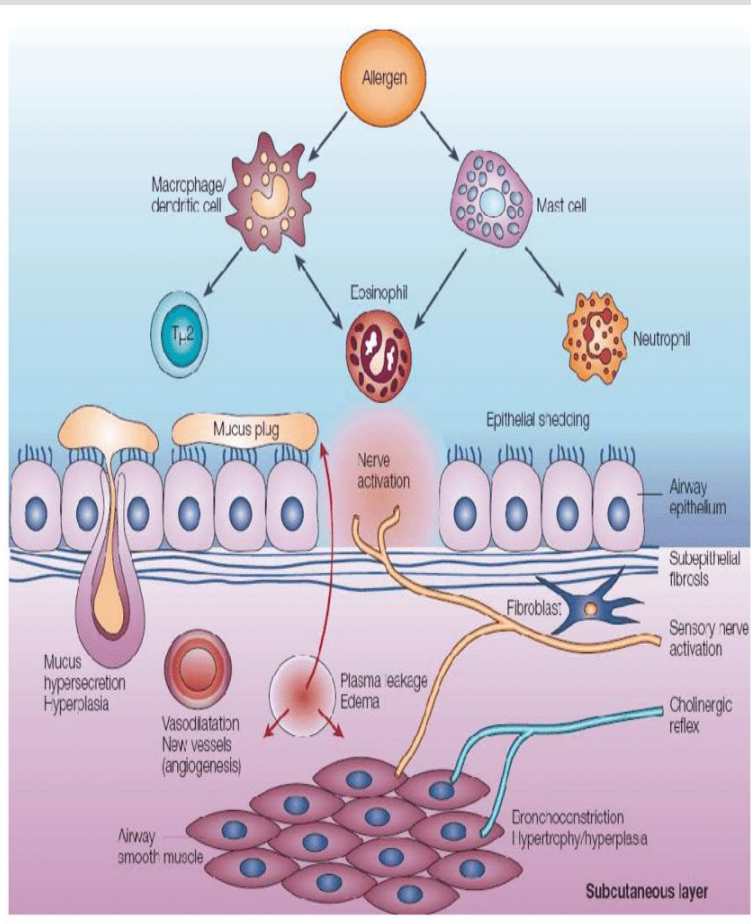


This is supported by the finding that EIB is attenuated when the inspired gas is more fully humidified and closer to body temperature



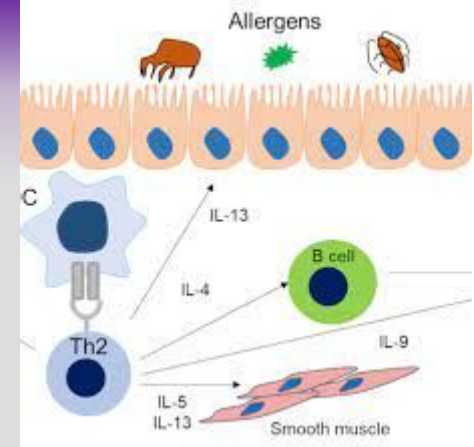
3- inflammatory mediators

Levels of bronchoconstrictive and inflammatory mediators are increased



leukotrienes LTC₄
LTD₄
histamine
interleukin (IL)-8

4- lymphocytes



Peripheral TH2-type lymphocytes are activated, with an increase in T cells expressing CD25 (IL-2R), and B cells expressing CD 23 .

These changes favor production of IgE and activation of eosinophils

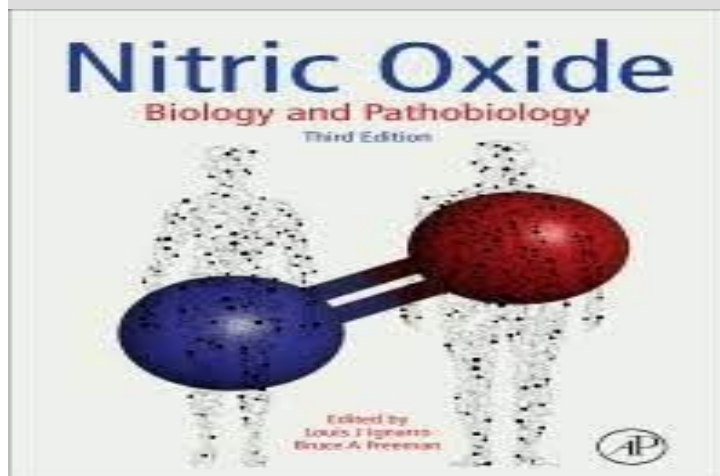
and activation of eosinophils

- Eosinophil influx and activation, measured using eosinophilic cationic protein levels, sputum eosinophils, or peripheral eosinophil counts, have been noted in some , but not all , studies of experimental EIB.

5-nitric oxide

exhaled nitric oxide (eNO) levels, which generally reflect airway inflammation

do not appear to correlate well with the development or severity of EIB



CLINICAL MANIFESTATIONS

Typical symptoms are

- shortness of breath
- chest tightness
- cough
- Wheezing

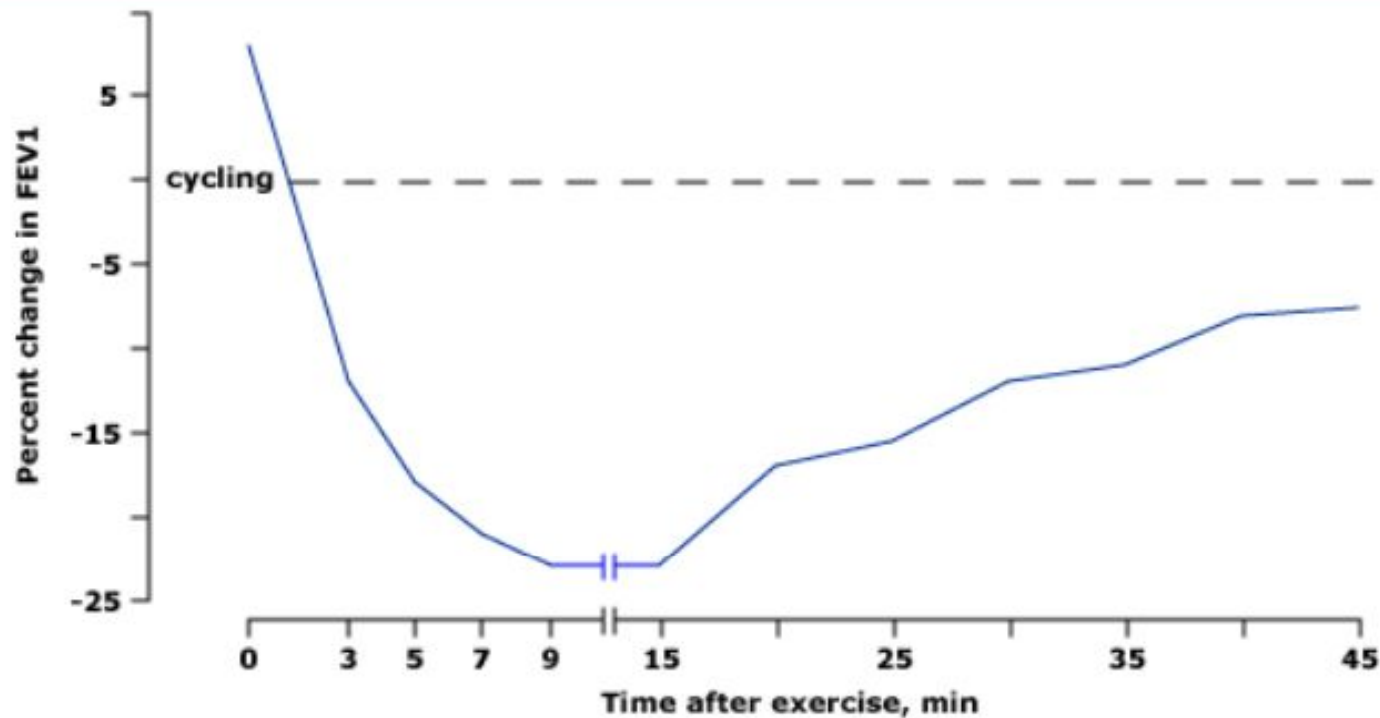
Patients with EIB typically have initial bronchodilation during six to eight minutes of exercise

The initial bronchodilation is followed by bronchoconstriction, which begins by three minutes after exercise

generally peaks within 10 to 15 minutes

resolves by 60 minutes

Exercise-induced bronchoconstriction



The time course of exercise-induced bronchoconstriction in an asthmatic patient in whom the FEV1 fell by more than 20 percent after cycling.

FEV1 fell by more than 20 percent

EIB IS different than **shortness of breath
related to exercise**

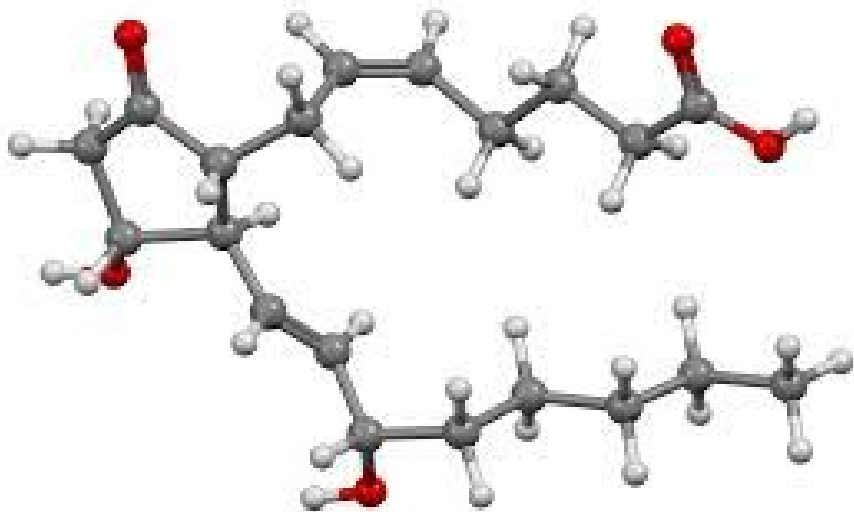
which generally resolves within **five minutes**
of stopping exercise

In most patients with EIB,
bronchoconstriction is followed by a
refractory period

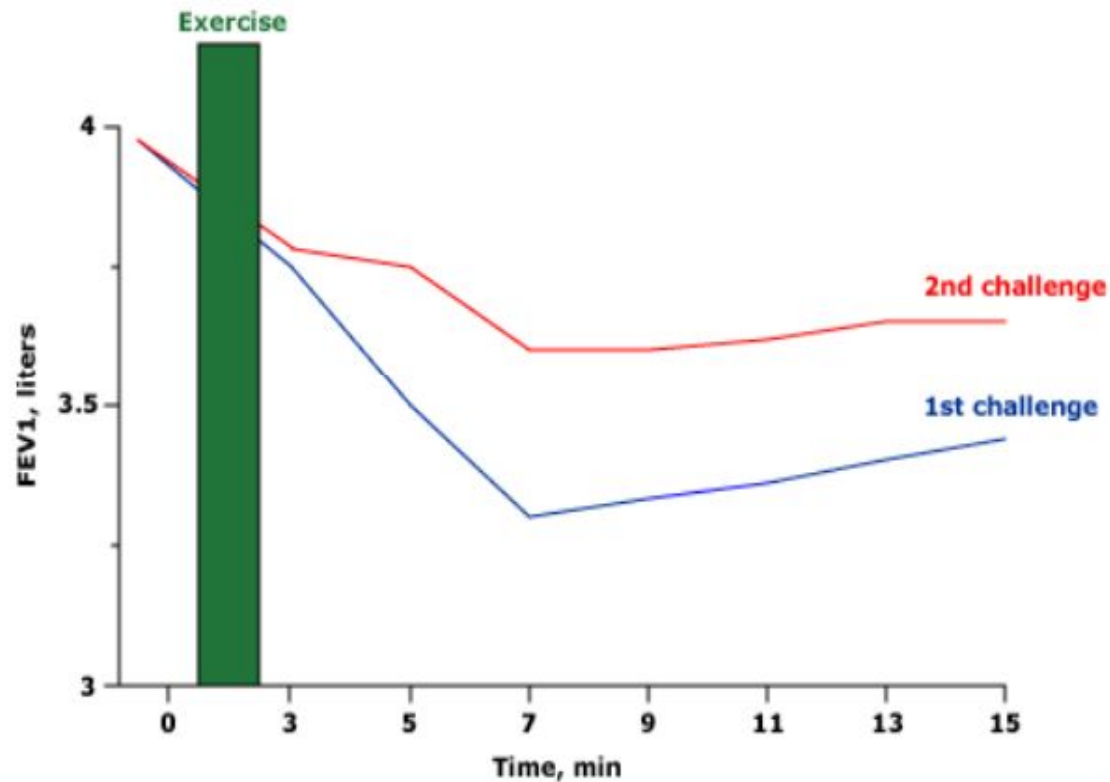
during which repeated exertion causes
less bronchoconstriction

This refractory period is generally
less than **four** hours

**Inhibitory prostaglandins
(particularly prostaglandin E2)
released during the refractory period
probably protect against repeated
episodes of EIB**



Refractoriness to repeated exercise-induced bronchoconstriction



Exercise-induced bronchoconstriction (as measured by a fall in FEV1) is attenuated when a second exercise challenge is performed one hour after an initial challenge.

DIAGNOSIS

In patients with **well documented asthma with typical asthma symptoms following exercise formal exercise testing is not needed unless symptoms do not resolve with, or are not prevented by, pretreatment with inhaled beta agonists.**

DIAGNOSIS

In patients **without documented asthma further assessment is helpful to ensure that alternative causes of dyspnea are not overlooked and that unnecessary therapy is not prescribed.**

DIAGNOSIS

- **This is particularly true when an adult develops new onset exercise related symptoms.**
- **Formal testing is also helpful in evaluating highly trained athletes, as exercise related respiratory symptoms are poor predictors of EIB in this setting**

An exercise challenge test is the most direct way to establish a diagnosis of EIB

This usually involves six to eight minutes of ergometer or treadmill exercise, sufficient to raise the heart rate to 85 percent of the predicted maximum.



An exercise challenge test is the most direct way to establish a diagnosis of EIB



A test is generally considered positive if the FEV1 falls by **10 percent** or more, although a fall of 15 percent is more diagnostic

surrogate tests to assess bronchial hyperresponsiveness
(eg, cold air hyperventilation, methacholine, histamine, or mannitol inhalation challenge)

**may be performed in specialized laboratories,
but **do not always** correlate with the presence
of EIB**





- Measurement of **peak expiratory flow** rates before and after exercise frequently leads to **inaccurate results**

- but portable devices that record forced expiratory volume in one second (**FEV1**) are more accurate

**After a baseline value has been established,
FEV1 can be measured before and 2.5, 5, 10, 15, and
30 minutes after exercise and correlated with
symptoms.**

Differential diagnosis

Other causes of exercise-induced dyspnea must be considered, particularly in patients who

- **have no other manifestations of asthma**
- **and derive no benefit from pretreatment with bronchodilators.**

Differential diagnosis

- **Central airway obstruction**
- **vocal cord dysfunction**
- **laryngotracheomalacia**
- **parenchymal pulmonary disease**
- **gastroesophageal reflux**
- **coronary heart disease**
- **heart failure**

- The differential diagnosis is similar among children. In one retrospective review, treadmill exercise testing was performed in 142 children referred to a pediatric allergy and pulmonology clinic with exercise-induced dyspnea who had no other signs of asthma or in whom treatment with beta-2-agonists had failed [39]. Symptoms of exercise-induced dyspnea were reproduced in 82 percent. Among these 117 children, only 11 (9 percent) had EIB (defined by reproduction of symptoms and ≥ 15 percent decrease in FEV1 from baseline). Other diagnoses included normal physiologic exercise limitation (63 percent), restrictive abnormalities (13 percent), vocal cord dysfunction (11 percent); laryngomalacia (2 percent), and hyperventilation and supraventricular tachycardia, each in one patient

MANAGEMENT

- **The combination of general measures and pharmacologic intervention can prevent EIB in almost all asthmatics.**
- **A major goal is to ensure that exercise is not avoided by patients with EIB.**

MANAGEMENT

- Asthmatics should exercise as much as desired
- and should be encouraged by the fact that athletes have won Olympic medals and played professional sports, in spite of symptomatic asthma

General measures

- Improved understanding of the **pathophysiology** of EIB has resulted in general recommendations that can help reduce its severity.

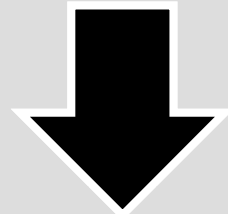
minute ventilation

Improving a patient's cardiovascular fitness reduces the minute ventilation required for a given level of exercise, thereby decreasing the stimulus for bronchoconstriction.



temperature and humidity of the inspired air

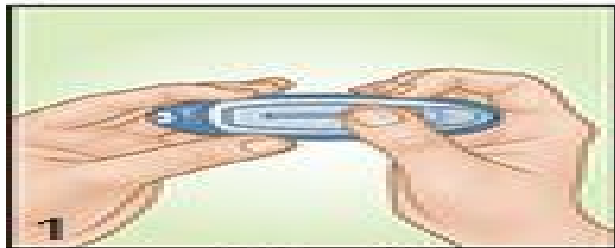
bronchoconstriction is lessened when the inspired gas is warmer and more humid



Patients should be instructed to breathe through a loosely fitting scarf or mask when exercising in cold, dry conditions

ensuring that patients know when and how to use a metered dose or dry powder inhaler correctly can greatly enhance the efficacy of pharmacologic measures

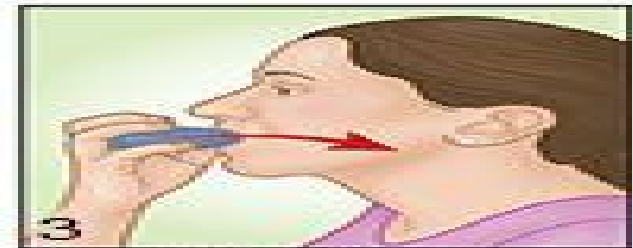
How to Use a Dry Powder Inhaler



1 Open inhaler



2 Breathe out



3 Breathe in



4 Hold your breath for 10 seconds



5 Breathe out slowly

Pharmacologic therapy

Pharmacologic therapy

- Treatment of EIB has been studied primarily in patients with both EIB **and** underlying asthma.
- Therapeutic options for patients with EIB as the **only** manifestation of airway hyperresponsiveness are less well researched.
- In general, if EIB occurs frequently in patients with poorly controlled asthma, the most important strategy is to improve overall asthma control .

Pharmacologic therapy

- Inhaled glucocorticoids and leukotriene-modifying agents are often useful in this regard. Prophylactic treatment of EIB prior to exercise, using inhaled beta-2 agonists and/or cromolyn sodium, should be considered in all patients with EIB, even if EIB is the sole manifestation of airway hyperresponsiveness.



Rapid-acting bronchodilators

Beta-agonists

- **All patients with significant EIB should be instructed to use prophylactic treatment approximately 5-20 minutes before exercise**
- **usually with two puffs of a rapid-acting inhaled beta-2 agonist (eg, albuterol) .**
- **This inhaler can also be used to relieve symptoms caused by exercise.**

- **Patients who require a preventive short-acting beta-agonist (SABA) once every day may also want to consider using one of these alternate agents**

However, both long-acting inhaled beta-2 agonists and regular use of short-acting inhaled beta-2 agonists provide less effective protection against EIB than does intermittent prophylactic use of beta-2 agonists

Long-acting bronchodilators

- Long-acting bronchodilators (LABAs), such as **salmeterol and formoterol**,
- work for *a* longer period than rapid-acting bronchodilators.

Formoterol

- Formoterol works as quickly as **albuterol** and lasts for **12 hours**
- so it is both a rapid-acting and a long-acting bronchodilator.

- **Combination inhalers containing formoterol can be used shortly before exercise (at least five minutes) and can also be used to relieve asthma symptoms that occur despite pretreatment.**

These medications *are* usually taken

twice daily

and **30 minutes** after the morning dose help prevent exercise-induced asthma symptoms for the next 12 hours.

➤ We do not recommend regular use of long-acting beta agonists as monotherapy for EIB, because of concerns about a loss of bronchoprotective effect over time .

➤ Thus, for patients who require regular dosing of a long-acting beta-agonist (LABA) to control EIB, we recommend concomitant use of **inhaled glucocorticoid** or cromolyn sodium, or an anti-leukotriene agent.

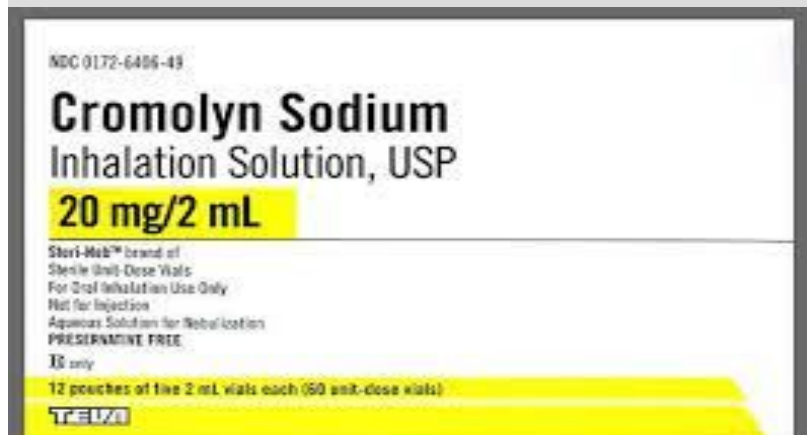


Children often present a difficult clinical situation by exercising vigorously and intermittently throughout the day without pretreating themselves prior to exercise.

In this setting, long-acting inhaled beta-2 agonists (such as salmeterol and formoterol) provide protection against EIB for most of the day

Cromoglycates

- An alternative approach is prophylactic use of inhaled cromolyn sodium (two to four puffs from a metered dose inhaler)
- taken 15 to 20 minutes before exercise .



Cromoglycates

- In exceptional situations, as with very high performance athletes or patients exercising in extreme conditions (eg, very cold, dry air), the combination of four puffs of an inhaled beta-2 agonist and four puffs of cromoglycate is likely to be more effective than either drug used alone, as demonstrated in a small randomized trial .

Inhaled glucocorticoids

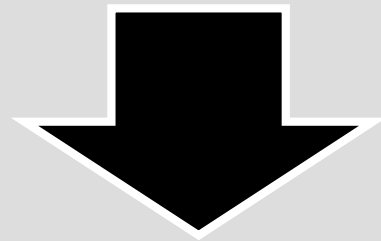
When poor asthma control is the cause of refractory exercise-induced bronchoconstriction, the most effective method of achieving asthma control involves use of inhaled glucocorticoids

Inhaled corticosteroids



**Although inhaled glucocorticoids will not improve EIB
in the short term**

they do improve airway hyperresponsiveness



**over weeks to months, decrease the magnitude of
bronchoconstriction that occurs with a given
workload**

- **Some studies have noted that inhaled glucocorticoids do not decrease EIB in a dose-related manner .**
- **In contrast, a decrease in methacholine sensitivity (as determined by methacholine challenge) is generally well-correlated with the inhaled glucocorticoid dose.**

This variability is partially explained by a greater magnitude of benefit from inhaled glucocorticoids in patients with higher sputum eosinophilia

Antileukotriene agents

Leukotriene modifying agents provide an attractive therapeutic alternative in the setting of chronic asthma complicated by EIB



Leukotriene modifiers work by **decreasing**
airway narrowing, inflammation,
and mucus production.

Antileukotriene agents

Urinary leukotrienes increase after exercise in patients with EIB

and treatment with montelukast attenuates this response, in addition to improving clinical control .

Antileukotriene agents

- Protection from EIB is apparent by **two hours** after a single dose of montelukast, and post-exercise recovery is accelerated .
- The long half-life of this agent allows once-daily dosing with durable protection from EIB for up to **12 hours** .
- However, leukotriene receptor antagonists are **not effective in all patients**

Leukotriene-modifying agents appear **superior to inhaled long-acting beta-2 agonists when treating asthmatics with EIB.**

**In one blinded multicenter trial, asthmatics with EIB
were randomly assigned to
either montelukast or salmeterol for eight weeks .**

**protective within three
days for both groups**

**by eight weeks,
the bronchoprotective
effect of montelukast
was significantly
better**

children with EIB can pose a therapeutic challenge

because they tend to exercise intermittently throughout the day and often neglect to premedicate with an inhaled beta agonist.

Antileukotrienes are an effective option in this setting

- **In a randomized, double blind study of EIB in children, montelukast and montelukast with budesonide were superior to budesonide and budesonide with formoterol**

- Examples of leukotriene modifiers include **montelukast** (Singulair) and **zafirlukast** (Accolate).
- These are taken in pill form by mouth once daily (montelukast) or twice daily (zafirlukast) and have few side effects.

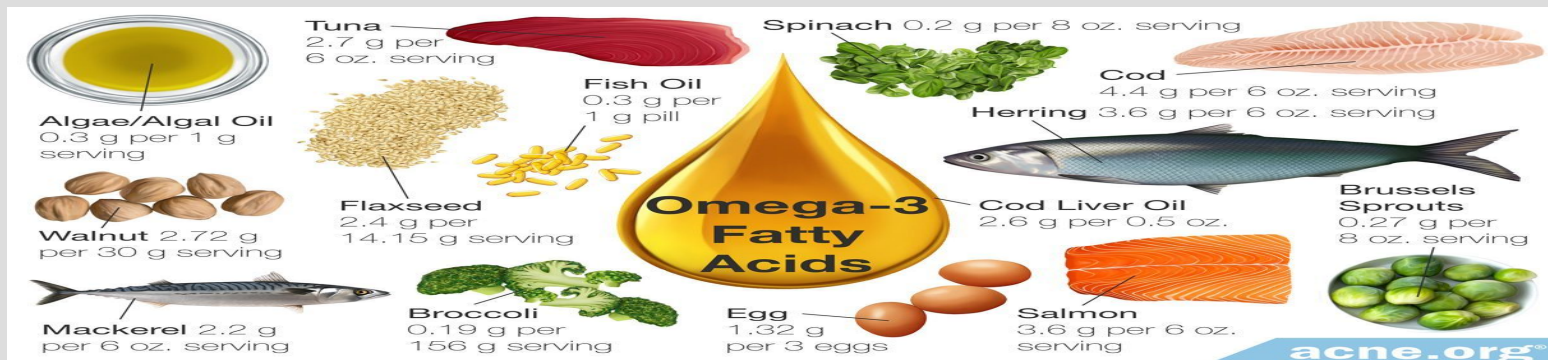
- **Montelukast** is approved for use **as needed** before exercise for patients who do not require daily medication.
- If not taken on a daily basis, montelukast should be taken at least **two hours** before the start of exercise.
- If the medication is taken daily, there is no need to take an additional dose prior to exercise

- Leukotriene modifiers are used for **prevention of symptoms, NOT for relief of symptoms once** they have developed.
- If asthma symptoms develop despite pretreatment with a leukotriene modifier, a rapid-acting bronchodilator (eg, albuterol, levalbuterol, or **budesonide-** formoterol) should be used

Dietary modification

Diets rich in anti-inflammatory omega-3 fatty acids

have **not** been conclusively demonstrated to
be **helpful** in the general population of
patients with asthma





patients with EIB

**three weeks with fish oil supplements
(containing omega-3 fatty acids)**

**had reduced leukotriene, PGD₂, IL-1 beta, and TNF
alpha in induced sputa.**

**Pulmonary function improved and bronchodilator
use was reduced.**

**This suggests that, in asthmatics with EIB, a diet
enriched with omega-3 fatty acids may be helpful**

Other therapies

- **Other types of asthma therapy are not very effective in protecting against EIB.**
- **As an example, oral beta-2 agonists and methylxanthines are marginally effective or ineffective in almost all patients**

- Several other drugs have been tested as possible prophylactic agents against EIB. Inhaled medications, including furosemide [75], prostaglandin E2 [76], indomethacin [77] and heparin [78], may protect against EIB. However, long-term clinical use of these compounds has not been directly compared with the prophylactic use of inhaled beta-2 agonists. For this reason, their role in clinical practice is unclear.

Breakthrough symptoms

- **If patients forget to take prophylactic therapy for EIB or if they experience breakthrough symptoms despite treatment, bronchoconstriction should be treated with two to four puffs of an inhaled beta-2 agonist.**
- **Cromolyn sodium is not effective in this situation**

Monitoring

- Response to therapy can be assessed subjectively in terms of symptom control and exercise tolerance.
- Peak expiratory flow measurement before and after exercise may be helpful.
- If objective measurement of a patient's response to therapy is required, a formal exercise test, rather than the more widely available methacholine challenge, should be considered



**THANK YOU
FOR
LISTENING**

