



Breathing Difficulties Among Adolescent Athletes – Previous Experience and Upcoming Threats

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Introduction

Exercise is one of the most common factors triggering cough, dyspnea, or breathing difficulties in otherwise healthy children. This condition is called Exercise-Induced Bronchoconstriction (EIB), a frequent phenomenon among early adolescent athletes. EIB symptoms include cough, wheeze, chest tightness, and dyspnea during or after physical activity. Physicians often underestimate the number of adolescents suffering from EIB; many athletes remain undiagnosed and untreated. In this article, we argue that the complexity of diagnosing EIB is greater for adolescent athletes than it is for adults due to a reduced capacity of adolescents to feel and understand symptoms. Furthermore, adolescents experience greater difficulty reporting any such symptoms of EIB to medical authorities.

Abstract

Adolescent athletes merit special medical attention. Recent literature highlights the growing problem of physical inactivity among young people while exploring various dimensions that may explain the lack of physical activity and potentially relevant interventions and strategies. There is growing evidence that physical inactivity predisposes to the development of asthma.

Exercise is one of the most common factors triggering breathing difficulties in otherwise healthy children. This condition is called Exercise-Induced Bronchoconstriction (EIB). EIB symptoms include cough, wheeze, chest tightness, and dyspnea during or after physical activity. In this article, we argue that the complexity of diagnosing EIB is greater for adolescent athletes than it is for adults. We want to draw the medical community's attention to EIB and asthma symptoms among adolescent athletes. We performed a meta-analysis of these two topics, consulting PubMed and Clinical Key for the terms: "Adolescent athletes," "exercise-induced bronchoconstriction," and "asthma in adolescent athletes." After analyzing the relevant scientific data, we list the most important facts and issues related to this population.

Chronic exposure to bronchospasm-inducing factors may be associated with the development of asthma. On the other hand, the beneficial effect of physical effort, especially for children with well-controlled symptoms, permits young people to perform physical exercises, even at the elite level [1].

This review aims to draw the medical community's attention to the problem of EIB and asthma symptoms among adolescent athletes. In the available medical literature, most data pertains to professional adult athletes. After analyzing the cited references, we describe the most critical issues affecting adolescent athletes.



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History of EIB

In the second century CE, Greek physician Aretaeus the Cappadocian wrote, "If from running, and exercise and labor of any kind a difficulty of breathing follows, it is termed asthma. "This reference may be the earliest known written report of EIB [2]. More recently, Salter published a book entitled "On asthma: its pathology and treatment" in 1860 [3]. Salter described various types of asthma with predisposing factors, dividing the disease into two types: spasmodic (i.e., idiopathic, uncomplicated) and organic (complicated). According to the author, "as exercise level increases, a rapid flow of fresh and cold air through the bronchi triggers organic asthma symptoms."

In the 1960s, researchers provided quantitative descriptions of bronchospasm during exercise. They observed decreased Forced Expiratory Volume in 1 Second (FEV₁) in certain patients with asthma during and after exercise. They described this phenomenon as Exercise-Induced Asthma (EIA) [4]. In later years, the term exercise-induced bronchospasm was used and finally become exercise-induced bronchoconstriction [5].

Definition of EIB

The definition of exercise-induced bronchoconstriction is the acute narrowing of the respiratory tract due to physical effort. This condition occurs both transiently and reversibly, which means that after a few minutes of stopping exercise, the airways' state typically returns to baseline [5]. EIB can occur both during and after exercise and can result in coughing, chest tightness, shortness of breath, and wheezing. The most significant airflow reduction usually occurs approximately 10 to 15 minutes after the start of exercise and may last up to 30 to 60 minutes before resolving. Typically, there is a relative refractory period; however, the repetition of physical activity within 60 minutes of the initial symptoms may cause recurrence of bronchoconstriction [6].

Furthermore, even healthy patients can manifest these symptoms, especially those performing strenuous physical activity [5,7]. For this reason, some researchers suggest that EIA and EIB are synonyms [8]. Others have stated that EIA occurs only in asthma-diagnosed patients, while EIB appears exclusively in those who do not present symptoms of asthma [9,10].

Some researchers question whether we underestimate the number of patients suffering from EIB and whether many such athletes remain undiagnosed or untreated [5,11]. Our findings suggest that reduced awareness of symptoms of early adolescents significantly hinders the diagnosis of EIB. Dickinson J et al. state that only 59% of athletes diagnosed with EIB self-reported at least one symptom. Some athletes do not report their symptoms due to concerns about losing their team status or showing "signs of weakness" [12]. Furthermore, athletes may not recognize EIB symptoms and misinterpret breathing difficulties as a regular part of their physical training. It is also worth noting that EIB presents in varying ways and that some athletes with EIB have normal respiratory test results. Rundell et al. support the finding by noting that athletes' symptoms are not related to the presence of bronchospasm. The proper diagnosis requires accurately assessing the patient's history, spirometry, and exercise challenge test results. Many physicians treat EIB based only on symptoms, without performing standardized exercise testing [13].

Pathogenesis of EIB

There are two proposed theories – osmotic and thermal – explaining the occurrence of EIB. The osmotic theory assumes that hyperventilation during physical effort leads to water loss from the respiratory epithelium's surface. This causes disorders in cell ion homeostasis and increasing mucus osmolarity. The respiratory tract wall contains mast cells and eosinophils that release inflammatory mediators, leading to bronchospasm when stimulated. A higher concentration of inflammatory cells in the sputum of patients suffering from EIB supports this theory.

The thermal theory assumes that the airways' heat loss with their subsequent reheating by incoming air after exercise may increase mucus secretion, swelling, and tissue inflammation, ultimately causing narrowing of the airways [1,9]. Additionally, cold air triggers the parasympathetic nervous system. This increase in vagal tone leads to bronchoconstriction with simultaneous constriction of the venous vessels to limit heat loss. At the end of physical effort, reflex dilatation of vessels occurs. All these factors ultimately lead to the narrowing of the airways, increasing their air-resistance [14].

Researchers suspect that chronic exposure to cold air during vigorous breathing causes EIB among competitive athletes practicing winter sports. This environmental exposure results in damage to the respiratory epithelium and interferes with its repair. In summer sports, chronic exposure to environmental allergens may result in elevated circulating levels of IgE [15].

Among swimmers, the added chemicals in the pool water may trigger EIB. During swimming, athletes inhale chlorine-rich water molecules above the swimming pool's surface, which irritates the respiratory tract. Repeated exposure to these substances can lead to inflammation, epithelial damage, EIB development, and asthma [1].

Additional causes of respiratory tract irritation in athletes include environmental factors, such as airborne allergens (e.g., pollen). Others report that people training in cold air (e.g., hockey, figure skaters, and speed skaters) may be more exposed to higher concentrations of Nitrogen Dioxide (NO₂) and particles left over by ice leveling machines. Athletes training on the streets, such as runners or cyclists, are more likely to inhale polluted street air [1].

Furthermore, among children who regularly play team games in the open air, there is a greater risk of developing asthma symptoms, especially in an ozone-rich environment. McConnell et al. observed a greater risk of developing asthma in athletes the more vigorous their training or, the more they spend time outside. Hyperventilation and breathing by mouth are conducive to ozone, which progressively reaches more distant parts of the respiratory tract. According to one study, patients who neglect their EIB symptoms may progress into the development of asthma because, over time, they experience airway remodeling [16].

Prevalence of EIB in young athletes

In the general population, about 5-20% have EIB. In children, the prevalence is 3-35%. The prevalence among adult elite athletes is higher, especially those at the Olympic-level (30-70%). These discrepancies may be due to the type of practiced sport, exposure to air pollution and allergens, and maximal exercise intensity achieved, which may vary depending on the sport season [5,17].

Medical providers often underestimate the prevalence of EIB among young competitors. A few studies report that EIB incidence in this group varies from 12% to 38% [1,5]. Jonckheere AC reports the prevalence of EIB is 33.3% in swimmers, 27.3% in basketball players, and 12.8% in football players [18]. Among young high school and college athletes in Mexico City, researchers, report an EIB frequency of 7.2%, with no differences between genders [7]. Ventura et al. indicated a frequency of self-reported EIB symptoms in young soccer players at 5.1% [19]. Bougault et al reported young soccer players with an EIB prevalence of 16% [11]. Among the undiagnosed young athletes suspected of EIB, the incidence was 29% [20].

Young weightlifters showed a high, 42.9% EIB prevalence. Authors claim that EIB is usually associated with sports-provoking elevated minute ventilation, but in this case, repetitive Valsalva maneuvers may be a risk factor in EIB diagnosis [7].

Diagnosis of EIB

Diagnosis of EIB among young athletes does not presently differ from adult athletes. On physical examination, especially at rest, patients suffering from EIB do not exhibit abnormalities [6]. Physicians can diagnose EIB by noting respiratory symptoms with exercise and confirming that suspicion through a standardized exercise challenge test [7].

There are several tests used to assess the occurrence of bronchospasm in EIB-positive athletes. One such test is spirometry. Importantly, spirometry alone cannot rule-out EIB given its high false-negative rate [5].

Regular exercise is a factor that improves the functions of the respiratory tract. Athletes possess higher cardiovascular and respiratory system parameters, meaning their baseline spirometry parameters can be higher than in the general population [17,21].

Provocation tests provide a basis for diagnosing bronchospasm during exercise and are divided into two groups: direct and indirect. The first group includes a methacholine challenge. This test uses methacholine to elicit a bronchospastic response of the respiratory tract. A fall in $FEV_1 \geq 20\%$ from the baseline value is considered positive [5,6].

Indirect tests consist of a treadmill exercise challenge, a free-running exercise challenge, Eucapnic Voluntary Hyperventilation (EVH), hypertonic saline challenge, and the mannitol test [5,6].

The most recommended indirect test is the American Thoracic Society-prescribed exercise challenge on a treadmill or a cycle ergometer. It consists of six to eight minutes of physical effort, with a heart rate target of 80% to 90% of maximal heart rate. The respiratory response is measured by performing repetitive spirometry, usually after 5, 10, 15, and 30 minutes of exercise [22]. The test is considered positive if there is a decrease in $FEV_1 \geq 10\%$ from the baseline value.

In the free-running exercise, the patient exercises for 6 minutes, and then the examiners repeatedly measure the patient's Peak Expiratory Flows (PEF). Subjects need to be motivated to maximize their effort to give more accurate results [23].

Eucapnic Voluntary Hyperventilation (EVH) is a study specially developed for EIB diagnosis that indirectly causes bronchospasm [5]. During the test, a patient must breathe for six minutes at 85% maximum voluntary ventilation rate with a con-

trolled concentration of carbon dioxide [6]. Inhaled air should contain 21% oxygen, 5% carbon dioxide, and 74% nitrogen. After three, five, 10, and 15 minutes, the examiner will assess the maximal voluntary flow-volume loops. As in the exercise challenge on the treadmill, EVH is positive if the FEV_1 shows a $\geq 10\%$ decrease from baseline [12]. EVB is the preferred diagnostic test used by many researchers because of the excellent standardization and sensitivity. Limitations of EVH include its requirement for special equipment and more demanding procedures, including proper training of testing personnel [6].

Two other indirect tests are inhalation tests using either hypertonic saline or mannitol. If there is a fall in $FEV_1 \geq 15\%$ compared to baseline, the test is positive [24,25].

Differential diagnosis

According to The American College of Chest Physicians (CHEST) guidelines and Expert Panel Report, the differential diagnosis of cough occurring in athletes over 12 years of age are EIB, asthma, respiratory tract infections, and upper airway cough syndrome due to rhinosinusitis. Providers should also consider environmental factors that may significantly affect lung function [26].

In a differential diagnosis of a young athlete presenting with breathing difficulties, physicians should consider exercise-induced Vocal Cord Dysfunction (VCD) when a patient exhibits laryngeal wheeze during physical effort, dyspnea, and cough, exercise-induced. Exercise-induced VCD affects up to 5-27% of patients previously mistakenly diagnosed with EIB. In such cases, physical effort creates a paradoxical motion of the vocal cords, especially during inspiration [1,27]. Physicians should consider VCD in any patient with difficult-to-treat asthma whose symptoms do not improve after treatment [6]. Exercise-induced laryngomalacia may present similarly. In either case, FEV_1 does not decrease after exercise or after the administration of β_2 -agonists or inhaled glucocorticoids [27].

In differentiating EIB among young athletes, providers should consider dysfunctional breathing (shallow breathing and lifting of the chest wall) as well as acquired and habitual breathing patterns. Dysfunctional breathing often occurs in people with asthma. Manifestations include the absence of any functional airway disorder, exercise-induced hyperventilation, and acute anxiety. As a result of hyperventilation, respiratory alkalosis occurs, causing dyspnea, light-headedness, chest tightness, and paraneesthesia's [6,27].

When investigating dyspnea, physicians should consider psychological factors, especially when working with young patients. Dyspnea is a subjective symptom and may be interpreted differently among various patients [27].

Rare pathologies causing exercise-induced symptoms, especially in adolescent athletes, include Hypertrophic Cardiomyopathy (HCM), which is the leading cause of sudden cardiac death in this group [6]. Other rare pathologies that simulate EIB symptoms include exercise-induced arrhythmias, cardiovascular dysfunctions, pulmonary embolism, anemia, interstitial lung disease, swimming induced pulmonary edema, exercise-induced anaphylaxis, and myopathies [27].

Young athletes in the light of new threats

At the end of 2019, few expected a new coronavirus – SARS-CoV-2 – whose outbreak appeared in Wuhan, China, would significantly affect the world population. After the World Health

Organization (WHO) announced a pandemic in March 2020, there was concern about patients who suffer from chronic diseases, including respiratory symptoms. Due to the on-going phase of the pandemic at the time of writing, we are likely to see many new research developments. In this section, we discuss a few early results.

Presently there is no evidence that asthma in children is a risk factor for infection with coronavirus disease 2019 (COVID-19). However, symptoms of COVID-19 can mimic asthma exacerbation, including dry cough and shortness of breath. Fever, which commonly occurs in COVID-19, could be a differentiating factor from asthma exacerbation. Furthermore, physicians should consider epidemiologic information such as travel history and possible contact with infected persons. From the limited data from the United States, children with symptoms of asthma should continue therapy. The Global Initiative for Asthma (GINA), the Centers for Disease Control and Prevention, and the North American Consensus Guideline on Allergy Care published statements that support this approach. Additional recommendations include frequent handwashing, apply the principle of social distancing, and avoiding airborne allergens.

Providers should pay special attention to athletes whose sports plans were canceled or postponed by this pandemic, including those with EIB and asthma. There is currently no data available on the prevalence, nature, and behavior of COVID-19 in athletes.

Consequences of isolation include increased sedentary behaviors, lack of communication among athletes and coaches, and insufficient exercise. Negative lifestyle changes can lead to inappropriate nutrition and increased body fat, which affects both physical and mental health. There is a global consensus that the beneficial effect of regular physical effort at moderate volume and intensity is associated with a decreased risk of respiratory infections. A sedentary lifestyle poses a more significant threat to athletes who depend on daily exercise. The restrictions put in place by governments to prevent the spread of COVID-19 limit an athlete's ability to train. At the time of writing, COVID-19 symptoms reported in pediatric patients are relatively mild, with recovery lasting 5-7 days. Nevertheless, experts recommend a period of prolonged rest once infected.

Jukic et al. offer strategies and solutions for athletes during the COVID-19 pandemic. Firstly, they recommend encouraging athletes to re-adapt their approach to isolation as an opportunity for "personal development." Secondly, by using the available technology, athletes should be supported and be in frequent contact with experts, such as coaches, nutritionists, physicians, and psychologists. Athletes need adequate equipment where they live, such as cardio equipment (e.g., treadmill, bicycle), resistance training equipment (e.g., dumbbells, elastic or medicine bands), and items to support exercises such as mats and foam rollers. Providers should counsel athletes to consider alternative sports skills training, such as using a kinesthetic ball for working out in small spaces. Furthermore, the physician should educate athletes about nutrition, supplementation, hydration, and encourage "preventive behaviors" (e.g., washing hands, social distancing). Every athlete should use forms of self-assessment and establish daily monitoring by the use of modern technology [28].

To summarize, athletes should comply with limitations and apply strategies that will allow them to maintain an appropriate level of physical exertion. Those who have asthma symptoms

should remain on their current medication and introduce precise control over the treatment. More research will be required to help improve these guidelines in the coming months [29,30].

A Growing problem with allergies

The majority of research related to sports and allergy focus on adult professional athletes, with few studies based on young athletes. Ventura et al. analyzed the population of young soccer players and reported a high prevalence of allergic diseases in this group. However, in comparison with control students, the results were not significantly different. This suggests that intensive training by soccer players is not related to a greater risk of allergic disease [11].

Bougault et al. reported that 49% of studied soccer players were allergic to at least one allergen, 33% self-reported allergies, and 16% had confirmed EIB. Conversely, many of these allergies are untreated. 44% of athletes believed that allergy treatments harmed their physical performance and could disqualify them from training. Some of these drugs are on the World Anti-Doping Agency (WADA) prohibited list. The study emphasizes the necessity to diagnose players with respiratory symptoms and screen asymptomatic athletes [11].

Quality of life in young athletes

Johansson et al. reported that compared to healthy adolescents, adolescents with EIB have more absences from school and respiratory symptoms during exercise. These factors may limit their motivation to improve physical activity [31].

Based on the Health-Related Quality of Life Survey (HRQoL), young girls who suffer from EIB scored lower in both respiratory function tests and HRQoL when compared to a population of EIB-negative girls. Boys did not show the same relationship. Moreover, girls with confirmed EIB had more sleep disturbances and significantly more anxiety scores than the healthy population [32]. Hallstrand et al. report that HRQoL results were substantially lower among adolescent athletes with previously confirmed EIB, mild asthma, and co-existing allergic rhinitis. Furthermore, the symptoms of dyspnea that appeared during exercise had a significant impact on the HRQoL result. Researchers suggest that proper treatment can improve the survey results and the quality of life of young people [33].

Among the surveyed children and adolescents at the EIB Landmark Survey, U.S. researchers found a higher prevalence of children avoiding exercises (31.8%) due to exercise-related symptoms [34].

However, when children with asthma symptoms took part in physical exercise, their quality of life improved [14]. Vahlkvist et al. reported less physical fitness in newly diagnosed asthmatic adolescents compared to control subjects. After one year of treatment, control of the disease and proper treatment both increased physical activity [35].

Non-pharmacological help for young athletes

Reducing symptoms of bronchospasm is not limited to the use of pharmacological methods. One of the non-pharmacological ways applicable to young athletes is the proper warm-up to induce a respiratory tract refractory period. Breathing moist pre-warmed air during exercise may reduce the risk of bronchoconstriction. In cold weather conditions, experts recommend face masks during training and sports competitions. According to ATS guidelines, proper warm-up before planned exer-

cise along with 10-15 minutes of moderately vigorous exercise (high-intensity interval or variable intensity warm-up exercise) can help to reduce this risk. Also, recommendations include limitation of exposure to allergens and air pollutants [22].

Studies showed a smaller decrease in FEV₁ during physical exercise, preceded by high-intensity interval or variable intensity warm-up, compared to no warm-up [36].

Pharmacological methods of EIB treatment

The ATS guidelines for the general population with EIB showed that EIB could be present in patients with and without confirmed asthma. They recommend taking a Short-Acting β_2 -Agonist (SABA) inhalation 5-20 minutes before a planned exercise. When SABA dosing is more frequent, but the patient still suffers from EIB symptoms, experts recommend daily monotherapy with Inhaled Corticosteroids (ICS), considered the most effective anti-inflammatory agents for EIB treatment. If necessary, one should use a Long-Acting β_2 -Agonist (LABA) [1]. Among the drugs with protective effects against EIB, formoterol (LABA) in dry powder inhalation can prevent EIB within a few minutes after administration for a duration of at least four hours [37]. Among athletes who rarely experience EIB episodes, it is sufficient to administer SABA before exercise.

Other recommendations include the daily use of a Leukotriene Receptor Antagonist (LTRA) taken about two hours before planned exercise. Its beneficial effects, however, are smaller than with a SABA or ICS. It is possible to use inhaled anticholinergic agents or a mast cell stabilizing agent before exercise as second-line therapy. Among patients suffering from EIB and allergies, adding an antihistamine is recommended [22].

Ducharme F. demonstrated that 400mcg/day of beclomethasone is more effective than leukotriene receptor antagonists in adults with mild or moderate asthma. The authors suggest that there is insufficient evidence to detect the efficacy of leukotriene antagonists among treated children. Still, others argue that anti-leukotriene drugs should remain a treatment option for the athletes with EIB when SABA and ICS therapy is insufficient [38].

The world doping agency

The World Doping Agency (WADA), an agency established in 1999 by the International Olympic Committee (IOC), fights doping among athletes and protects the integrity of sport against using illicit substances. Every year WADA publishes a list of prohibited drugs, including β_2 -agonists and ICS, treatments for athletes suffering from EIB and Asthma. These substances are considered to be performance-enhancing drugs [1,34].

Although these drugs are not allowed to be used in systemic administration by athletes, under certain conditions, the IOC does permit its use in athletes who suffer from EIB and asthma. The IOC regulations require a diagnosis of AHR or proof that bronchodilators reverse bronchoconstriction to use these drugs in competition. Pharmaceuticals from this group include (inhaled): formoterol, salbutamol, terbutaline, and salmeterol. Furthermore, athletes must notify WADA or the IOC Medical Commission if prescribed ICS treatment [1].

Summary

Our review has revealed that EIB is under-diagnosed and under-treated in young athletes [11]. The standard for diagnosis is both respiratory symptoms with exercise and a proper exercise challenge test. Even athletes who refrain from reporting symp-

toms experience a decline in lung function performance after exercise [5,13].

Nonetheless, it is essential to avoid over-diagnosing EIB, which may lead to overtreatment. Limited access to relevant provocation tests can contribute to a lack of awareness and misdiagnosis of EIB, as asthma and other diseases produce similar symptoms [5].

Appropriate treatment for the diagnosis of EIB in young athletes should be associated with regular control visits [1].

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