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## Key points

- “Dyspnoea” during exercise is a common complaint in seemingly otherwise healthy athletes, which may be associated with fatigue and underperformance.
- Because dyspnoea is an general term and may be caused by numerous factors, ranging from poor aerobic fitness to serious, potentially fatal respiratory and nonrespiratory pathologies, it is important for clinicians to obtain an appropriate case history and ask relevant exercise-specific questions to fully characterise the nature of the complaint so that a targeted diagnostic plan can be developed.
- Exercise-induced bronchoconstriction and exercise-induced laryngeal obstruction are two common causes of dyspnoea in athletes, and both are regularly misdiagnosed and mismanaged due to poor adherence to available practice parameters.
- Aside from airway dysfunction, iron deficiency and anaemia, infectious disease, and musculoskeletal conditions are common problems in athletes which ultimately may lead to complaints of dyspnoea.

## Educational aims

- To inform readers of the common causes of dyspnoea encountered in athletes.
- To highlight that airway diseases, such as asthma and exercise-induced bronchoconstriction, are commonly misdiagnosed and mismanaged.
- To introduce readers to common nonairway causes of dyspnoea in athletes, including clinical features and general principles of diagnosis, and management.
- To emphasise the importance of a detailed case history and proper adherence to established protocols in evaluating and managing the dyspnoeic athlete.
- To provide readers with a general framework of appropriate questions that are useful for developing a targeted diagnostic plan for evaluating dyspnoeic athletes.



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# Common causes of dyspnoea in athletes: a practical approach for diagnosis and management

Dyspnoea during exercise is a common chief complaint in athletes and active individuals. It is not uncommon for dyspnoeic athletes to be diagnosed with asthma, “exercise-induced asthma” or exercise-induced bronchoconstriction based on their symptoms, but this strategy regularly leads to misdiagnosis and improper patient management. Dyspnoea during exercise can ultimately be caused by numerous respiratory and nonrespiratory conditions, ranging from nonpathological to potentially fatal in severity. As such it is important for healthcare providers to be familiar with the many factors that can cause dyspnoea during exercise in seemingly otherwise-healthy individuals and have a general understanding of the clinical approach to this patient population. This article reviews common conditions that ultimately cause athletes to report dyspnoea and associated symptoms, and provides insight for developing an efficient diagnostic plan.

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**Dyspnoea, fatigue and underperformance are often interrelated symptoms in athletes, and may have various causes** <http://ow.ly/4nsYnk>

## Introduction

Dyspnoea is a common cause of concern in athletes, and clinicians in a variety of healthcare settings are likely to encounter active individuals with a chief complaint that can be generalised into this category. There are a number of conditions that can ultimately result in athletes having “difficulty breathing” or “shortness of breath”, or other symptoms seemingly related to respiratory dysfunction. When one considers the physiological demands of exercise, it is logical that the underlying cause(s) of dyspnoea may ultimately be rooted anywhere within the process of oxygen transport from the ambient air into the working muscles. As such, dyspnoea during exercise may be directly

associated with the respiratory system or may result from suboptimal function of oxygen transport that ultimately leads to greater than normal ventilation. Additionally, dyspnoea may be associated with musculoskeletal factors involved in the mechanics of breathing. Given that dyspnoea ultimately describes a sensation perceived by the patient, it may be somewhat subjective and does not always indicate pathology. Clearly, a multitude of factors create challenges in evaluating athletes with dyspnoea. Here, we aim to provide an overview of common reasons athletes and seemingly otherwise-healthy physically active individuals present with symptoms associated with dyspnoea in nonemergency settings, an overview of the approach to diagnosing these patients, general



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tenets of patient management and common pitfalls in working with dyspnoeic athletes.

## General approach to the dyspnoeic athlete

Patients may use terms associated with dyspnoea, fatigue and underperformance in an interchangeable manner, and therefore it is often necessary to clarify the chief complaint so that an appropriate diagnostic pathway can be determined. Indeed, these types of symptomatic descriptors may all be inter-related and coexist within an individual, but each may also occur separately. This is illustrated in the following examples.

- Athlete A may think that they “tire prematurely” during practice compared to the other players because they need to stop for breaks to catch their breath. Athlete A may present with a chief complaint of “fatigue” or “underperformance”, which may ultimately be rooted in a previously undiagnosed obstructive airway disease.
- Athlete B may present with a chief complaint of “shortness of breath” because they also have to stop frequently to catch their breath. However, athlete B may simply lack the physical fitness of their teammates.
- Athlete C may present with a chief complaint of “shortness of breath” because they also have to stop frequently catch their breath. Although this athlete reports the same symptoms as athlete B, athlete C may have a previously undiagnosed cardiovascular disease.

In these examples, all three athletes report similar symptoms (needing to stop often to catch their breath) but their primary reason for seeking medical care differed (“fatigue” *versus* “shortness of breath”). Likewise, two of these hypothetical individuals have a pathological condition but one does not. Given the vague or ambiguous terminology used to describe symptoms often associated with dyspnoea in athletes, clinicians must gather sufficient detail from the patient to discriminate between each of these factors in attempt to characterise the nature of dyspnoea. This information may be used to narrow the differential diagnosis list so that the clinician can focus on the most likely causes of dyspnoea for a given individual. To do this, clinicians must obtain a thorough case history through asking appropriate questions which are specific to the exercise associated dyspnoea (table 1).

In the previous examples, all three athletes experienced similar symptoms during exercise, despite different physiological mechanisms. Parents, coaches, athletes and even healthcare providers may recognise common traits between various athletes, and assume that each individual

has the same cause of dyspnoea (and requires the same treatment). Using the previous example, athlete A may have been diagnosed with asthma and appropriately prescribed a bronchodilator/anti-inflammatory inhaler to manage dyspnoeic symptoms. Other team mates experiencing similar symptoms may believe they also have asthma and seek similar treatment for it. If healthcare providers simply assume that athletes B and C also both have asthma, and prescribe inhalers to these athletes, athlete B is unnecessarily medicated and potentially dangerous cardiovascular disease continues to remain undiagnosed in athlete C. Alternatively, it is possible for poor physical fitness to incorrectly be viewed as the reason for dyspnoea, such that athletes with potentially serious pathological conditions that need treatment may simply be encouraged just to try harder, do more training, be patient and hope that it resolves itself, or simply give up.

Clearly, it is important that clinicians minimise assumptions for each individual case and not be biased by unofficial suspected diagnoses. This scenario of diagnosing athletes with asthma and prescribing an inhaler based on common symptoms of dyspnoea may seem completely reasonable to some but highly inappropriate to others. It is nonetheless a common approach, which ultimately results in many misdiagnosed and unsuccessfully treated athletes. In the following sections, we will discuss common types of airway dysfunction, conditions that may imitate it and various other conditions that may cause an athlete to present with a chief complaint of dyspnoea.

## Asthma and exercise-induced bronchoconstriction

Athletes presenting with dyspnoea are often initially suspected to have asthma or “exercise-induced asthma” based on their reported symptoms and clinical history. Often, diagnosis is (inappropriately) based on signs and symptoms alone, and these individuals are provided a bronchodilator inhaler and instructed to use it before performing activity. However, this paradigm is inappropriate for a number of reasons described in the following sections.

### Definitions

Asthma is a chronic airway disease characterised airway inflammation and reversible bronchoconstriction, which may eventually result in airway remodelling. Given the diversity of asthma phenotypes, “asthma” or “asthma syndrome” may be considered an umbrella term for a wide array of lower airway diseases [1]. Asthma attacks may be triggered by exercise as well as numerous other factors, such as airborne allergens (*e.g.* pollen

**Table 1** Questions to ask athletes and physically active individuals presenting with a complaint of dyspnoea during exercise

Question/request	Rationale
<b>General symptoms and history</b>	
Please describe your symptoms in detail	It is useful to have athletes attempt to first describe their symptoms without any leading questions that can bias their account Important information such as the presence of respiratory noises, fatigue/malaise, time of onset and factors that exacerbate the condition may be noted
Please describe what your breathing feels like when you experience these symptoms	“Dyspnoea” is a general term, so identifying specific sensations such as sharp pain, dull ache, chest tightness, difficulty inspiring, difficulty expiring, <i>etc.</i> , may provide some insight into the nature of the issue
When did you first notice these symptoms?	This information may be connected to a specific event ( <i>e.g.</i> trauma during a game, beginning or discontinuation a medication or a change in environment/location); for instance, a change in performance level (recreational team to competitive team) may indicate higher intensity or duration of exercise, or psychological factors ( <i>i.e.</i> competition anxiety)
Did you note any specific incidents or changes in your routine associated with this time period?	
Do you only experience these symptoms during exercise, and not at rest?	Symptoms experienced only during exercise generally suggest that exercise itself is a triggering event ( <i>e.g.</i> EIB without asthma) Suspicion of exercise as a trigger for symptoms should prompt more specific questions related to the exercise itself; however, it is also possible for some conditions to first be noticed only during exercise (when cardiorespiratory demands are greatest) and then eventually progress to being present at rest
Do you experience any symptoms in your heart, such as chest tightness, chest pain, unusually rapid pulse or unusual heart rhythms?	A feeling of chest tightness is common in asthma and EIB but may also be present in other cardiopulmonary conditions ( <i>e.g.</i> , pericarditis) The presence of actual pain should be investigated further to determine if it is cardiopulmonary ( <i>e.g.</i> ischaemia) or musculoskeletal ( <i>e.g.</i> costochondritis) in origin Although athletes with noticeable dysrhythmias ( <i>e.g.</i> supraventricular tachycardia) are likely to describe their symptoms as a chief complaint, it may be useful to confirm that the patient is not experiencing such symptoms
Did the symptoms come on suddenly or did they develop gradually over time?	This may be useful for identifying acute conditions, such as spontaneous pneumothorax, dyspnoea associated with trauma, <i>etc</i>
Are your symptoms becoming more severe or have you developed new symptoms beyond your breathing issues?	This may provide some insight into the time course of the condition and whether it is systemic ( <i>i.e.</i> infectious disease) or localised ( <i>i.e.</i> EILO); for instance, overtraining syndrome and infectious diseases may initially cause shortness of breath during high-intensity exercise but progress to new symptoms such as general fatigue and muscle pain
Is breathing painful, and if so, where is the pain?	Some causes of dyspnoea are associated with pain ( <i>e.g.</i> pneumothorax and costochondritis) whereas EIB and EILO generally are not
Have you recently experienced any physical trauma ( <i>e.g.</i> tackles in football or an automobile accident)?	Muscular contusions or tears, joint dislocations and skeletal fractures that could influence the mechanics of breathing must be considered

Continued

Table 1 Continued

Question/request	Rationale
Do you ever feel lightheaded or dizzy while experiencing these symptoms?	These symptoms suggests the individual may be developing hypoxaemia ( <i>e.g.</i> inadequate alveolar gas exchange) or inadequate blood flow to the brain during exercise ( <i>e.g.</i> inadequate blood pressure or vertebrobasilar artery insufficiency)
Aside from your respiratory symptoms, have you been feeling unusually tired or exhausted when you are not exercising?	Overtraining syndrome and infectious disease ( <i>e.g.</i> Lyme disease, mononucleosis or influenza) are common and may contribute to general fatigue, malaise and unusual soreness Emotional illness ( <i>e.g.</i> clinical depression) may also be considered Less common conditions that influence metabolic dysfunction ( <i>e.g.</i> mitochondrial myopathy) may also be considered
Do you have unusual muscle or joint pain, beyond what you would normally expect from exercise?	
<b>Exercise-specific symptoms</b>	
How long have you been doing the type of exercise in which you experience these symptoms?	It is important to understand the individual's reference point for the dyspnoeic symptoms reported; for instance, an individual with a long history of recreational running is likely to be familiar with their ventilatory response during running, whereas they may feel unusually out of breath in unaccustomed forms exercise with different neuromuscular demands ( <i>e.g.</i> swimming) or intensity ( <i>e.g.</i> sprint-interval sports like soccer)
Have you recently advanced to a higher level of participation ( <i>e.g.</i> changed from a junior high school team to high school team, or started with a college team)?	Athletes who have recently moved up to a higher level of participation may simply be less fit than the others around them, and therefore be breathing significantly harder and feel they are underperforming as a result
Do you wheeze or make noises during breathing?# If so, do you think it is during inhalation or exhalation?	Expiratory wheezing is common in asthma and EIB A high pitched inspiratory stridor is common in EILO The presence of these noises should lead to appropriate diagnostic methods for the respective condition; however, EIB and EILO may occur without these noises EIB and EILO can also be comorbid with one another
Do you only experience these symptoms during certain types of exercise?	If certain types of exercise are tolerable but others are not, clinicians should try to identify differentiating factors; for instance, exercise posture and musculoskeletal demands can influence symptoms in dyspnoea of musculoskeletal origin ( <i>e.g.</i> upper body movement during running may aggravate costochondritis but cycling at a similar intensity may not cause signs of dyspnoea) Additionally, environmental factors may also be identified ( <i>e.g.</i> athletes with EIB may experience symptoms while running outdoors but not during stationary cycling indoors due to differences in ambient air)
Are the symptoms consistent each time you exercise or do they vary from day to day?	This can provide further insight into possible triggering factors ( <i>e.g.</i> environmental conditions, venue, exercise type, exercise intensity and psychological stress)
Do these symptoms occur during practice, competition or both?	Psychogenic factors may contribute to dyspnoea, including anxiety during competition In addition to psychological factors, exercise-intensity, exercise duration and venue/environment may also account for differences between practice and competition

Continued

Table 1 Continued

Question/request	Rationale
<b>Environment-specific questions</b>	
Do your symptoms seem better or worse in any specific type of weather or season of the year?	Allergies and rhinoconjunctivitis may cause dyspnoea themselves or trigger seasonal EIB Humidity can also influence airway responses ( <i>i.e.</i> dry air can trigger EIB) Athletes may also switch between venues between different times of year ( <i>e.g.</i> more indoor training in during certain periods), which could introduce periodic variation in dyspnoea symptoms
Do your symptoms seem better or worse at any specific location?	Airborne pollutants, such as vehicular exhaust from fossil-fuelled automobiles and ice resurfacers, may trigger airway responses Likewise, indoor pools with high levels of chloramines may also trigger airway responses Certain venues may also contain other respiratory irritants ( <i>e.g.</i> chalk dust at gymnastics centres and climbing gyms) Different venues for the same sport may have large variability in air quality ( <i>i.e.</i> electric ice resurfacers, dust collection systems and nonchlorine filtration systems), which can account for differences in symptoms between sites
<b>Other questions</b>	
Have you donated blood, had surgery or experienced any major blood loss recently?	While the latter two questions should be obvious, they should be included if other suspected causes are not obvious
Is it possible that you are pregnant?	In the early stages of pregnancy, athletes may not yet be aware they are pregnant
Do you enjoy the exercise/sport/activity you are doing?	
What is your motivation for doing the exercise/sport/activity?	Although unusual, some individuals may simply no longer want to participate in a specific activity and attempt to find a medical excuse to limit/end participation Answers to these questions may be biased in the presence of a parent, coach, team member or other influential individual

Responses to these questions are meant to provide guidance for determining the most likely differential diagnoses to pursue through further diagnostic testing procedures. Diagnosis should not be based on reported symptoms and question responses alone, due to poor diagnostic accuracy. Rather, these questions should be viewed as additional questions beyond those routinely asked during a clinical exam (*i.e.* personal medical history, family medical history, medication use, *etc.*). Additionally, responses to these types of questions may be useful in determining whether interventions are successful and whether the condition is progressing positively or negatively over time. EIB: exercise-induced bronchoconstriction; EILO: exercise-induced laryngeal obstruction. #: Including demonstration of such noises if possible.

or pet dander), respiratory irritants (*e.g.* vehicular air pollution or tobacco smoke), environmental factors (*e.g.* dry air), infectious disease, psychological events, various behaviours and other stimuli [2, 3]. Bronchoconstriction that occurs shortly after (or in some cases, during) exercise is specifically referred to as exercise-induced bronchoconstriction (EIB) and is relatively common in individuals with asthma. However, EIB may also occur in nonasthmatic individuals and, therefore, it is not appropriate to refer to the condition as “exercise-induced asthma”, since the other characteristics of asthma may not be present.

## Epidemiology and misdiagnosis

EIB is commonly diagnosed in active individuals who report symptoms of dyspnoea, fatigue or inferior performance during exercise. EIB occurs across ages and fitness levels [4, 5]. The prevalence is reported prevalence ranges from ~10 to >50% or greater in competitive athletes [4, 6, 7]. Guidelines for diagnosis and management of asthma [8] and EIB [7, 9–11] are well established. However, asthma and EIB are frequently misdiagnosed in clinical practice [12], in part because diagnosis is typically made based on symptoms alone

(as in the previous examples), rather than strictly adhering to proper diagnostic algorithms [13]. The signs and symptoms of EIB are very nonspecific and therefore have poor clinical diagnostic value. Inappropriate diagnosis and management of EIB can lead to continuation or progression of symptoms, which may lead to impaired performance, discontinuation of sport or in extreme cases, sudden death [14, 15]. Case reports abound in which a serious condition was initially missed due to a misdiagnosis of EIB [16].

A recent multicentre study found that adherence to asthma guidelines was quite poor for children and adults in primary care centres throughout the USA [17]. Misdiagnosis and improper management of asthma and EIB in athletes is well described in the literature, and is evidenced by the large number of athletes who use prescription bronchodilators inhalers who test negative for EIB and the many athletes who report unresolved symptoms despite use of such inhalers [18]. The latter category suggests that improper management and other conditions besides EIB are often responsible for dyspnoea in athletes. Numerous studies have reported examples of athletes diagnosed with “asthma” without pulmonary function testing, and generally, many of these athletes are found to be misdiagnosed [13].

Misdiagnosis is only one issue that causes poor responses to treatment to airway disease. A study in children found that, although only 4.2% of the children were misdiagnosed, 19.7% had comorbidities [19], which emphasises the need to thoroughly evaluate the patient and perform regular follow-ups to verify successful treatment. In other words, diagnosis and management of asthma or EIB may not fully resolve dyspnoea, as comorbidities may also occur.

### Diagnostic protocols

Given the high incidence of asthma and EIB, and its widespread false-positive and false-negative misdiagnoses, it is imperative that clinicians understand the signs and symptoms of both conditions, proper diagnostic procedures, and other conditions that can imitate them. Accurate spirometry measurements are essential for the diagnosis of asthma and EIB, and detailed consensus statements and practice parameters are available for this purpose. Athletes who have normal spirometry at rest should undergo spirometry following a test designed to elicit a bronchoconstriction response. There are generally three ways to do this, with detailed protocols available elsewhere: 1) dry-air exercise challenge [20–22]; 2) eucapnic hyperpnoea [23]; or 3) an inhaled respiratory desiccant (*i.e.* mannitol) [24, 25]. There are also a number of other challenge tests available, which use both indirect and direct stimulation to provoke an airway response.

Exercise testing and eucapnic voluntary hyperpnoea should both replicate the ventilatory demands of exercise, and thus must be of sufficient intensity and duration (~6–8 min) to elicit an EIB response if one is present. Dry air is necessary to ensure optimal diagnostic accuracy, as the pathophysiology of EIB is rooted in dehydration of the respiratory mucosa, which results in release of inflammatory cytokines that trigger bronchoconstriction. The diagnostic accuracy for these challenge tests has been well established, so it is necessary to perform them in accordance with the recommended protocols without modification [11]. Withholding schedules for medications must be properly followed [26]. Additionally, some athletes who are positive for EIB may sometimes test negative and thus two tests may be required [27]. Likewise, seasonal allergens may influence test results [28] and therefore diagnostic testing should be performed during the time of year that the individual is experiencing symptoms.

### Management protocols

Pharmacological management of asthma and EIB has been extensively researched and detailed management protocols are well established [9–11, 29, 30]. Generally, inhaled short-acting  $\beta$ -agonist (SABA) bronchodilators should be the initial treatment of choice for individuals with EIB. These should only be used in response to an EIB episode or up to 2–4 times per week ahead of exercise likely to induce an EIB bout. Daily use of SABA can quickly result in tolerance and limits its effectiveness. Therefore, SABA should not be used on a daily basis. Leukotriene receptor antagonists may also be added to the management protocol.

If the athlete's symptoms are sufficiently severe that they feel daily use is necessary, the situation should be further evaluated to determine if the medication is being used correctly and whether the condition is more severe than originally thought. Combination therapy of bronchodilators and inhaled corticosteroids is used when airway inflammation is present. Although therapy-resistant asthma does exist, a thorough examination of the situation can resolve many cases in which response to treatment is suboptimal. For instance, a study in asthmatic children found that very few individuals truly had therapy-resistant asthma, but rather, poor adherence, improper inhaler technique and ongoing exposure to environmental triggers were the key reasons for improper response to treatment [19].

A number of nonpharmacological management options have been suggested, including vitamin C, fish oil and lycopene supplements, but the available evidence for these interventions is generally limited and weaker than pharmacological options [10]. Sprint-interval exercise may be an effective warm-up for individuals with mild EIB, as it can cause bronchoconstriction initially, which is

followed by a refractory period during which normal airway function may be achieved [31].

## Exercise-induced laryngeal obstruction and vocal cord dysfunction

Exercise-induced laryngeal obstruction (EILO), formerly referred to as vocal cord dysfunction (VCD), is one of the primary imitators of asthma and EIB. EILO is commonly misdiagnosed due to its overriding symptoms with asthma and EIB. Indeed, one study reported the average time to correctly diagnose EILO after the onset of symptoms was 4.5 years [32]. As such, a number of individuals who have EILO are inappropriately treated with bronchodilator and/or anti-inflammatory inhalers. Given that bronchoconstriction and airway inflammation are not the primary cause of dyspnoea in these individuals, pharmacotherapeutic interventions for asthma and EIB are generally unsuccessful in these patients [33]. A recent study confirmed there is significant morbidity and economic cost associated with mistaking these conditions for asthma [34].

### Definitions

Although the VCD term is prominent in the literature and still may be used by some, a recent consensus statement suggested that EILO is more appropriate, as many of the laryngeal conditions classified as VCD did not necessarily represent actual dysfunction of the vocal cords [35]. Numerous other related terms may also be categorised as EILO, such as paradoxical vocal fold motion disorder [35]. EILO is a more accurate umbrella term to represent conditions that cause obstruction of the larynx during exercise. EILO is characterised by abnormal closure at the supraglottic and/or glottic level of the larynx, generally during inspiration [35], which causes resistive airflow associated with shortness of breath and dyspnoea [36, 37]. The term “inducible” specifically suggests that the obstruction is not present at rest and is triggered by a specific stimulus [35]. The confusing nature of the nomenclature on laryngeal obstruction may complicate communication between clinicians and has served as a barrier to synthesis of research about this condition. A number of other conditions of the oropharynx, larynx and trachea can mimic EILO [38].

### Epidemiology

EILO may be present in ~5% of the athletic population [4, 33]. One study identified 35% of athletes referred for dyspnoea evaluation had EILO [39], while another suggested the prevalence may be as high as 70% of referred patients [13]. Some studies indicate EILO is more common in females and adolescents, and subjects and symptoms

associated with EILO, such as inspiratory stridor and dyspnoea, seem to be more prevalent in athletes participating in outdoor sports [13, 33, 39]. Although EIB and EILO may exist separately, they are often comorbid [4]. In numerous studies, approximately one-third to one-half of the participants with EILO also had EIB [4, 13, 33, 40, 41]; however, this does not imply that they are dependent on each other since EILO dyspnoea originates from the larynx and EIB dyspnoea is through the chest with no sign of laryngeal dysfunction [42].

### Diagnosis

Symptoms of EILO include dyspnoea, inspiratory stridor, shortness of breath, throat tightness, voice changes and chest tightness [13, 32, 33, 41]. Objective diagnosis of EILO is best achieved through direct visualisation of the larynx. Patients with EILO may be asymptomatic at rest and therefore have a false-negative test result if laryngeal examination is not performed during exercise [43]. Thus, continuous laryngeal endoscopy (CLE) during exercise allows for uninterrupted visualisation while the patient is symptomatic (*i.e.* during exercise) [44]. During CLE, the sign of EILO is apparent because it shows a direct view of the inflammation/irritation with abnormal vocal fold and/or aryepiglottic fold motion [45] and the patient may demonstrate high-pitched inspiratory stridor with dyspnoea [37]. During laryngoscopy, the patient ultimately has a decrease in the cross-sectional area of the larynx which causes dyspnoea [45]. While completing the laryngoscopy, it is important to note key findings throughout the visualisation such as the location (supraglottic, glottic or subglottic), expiratory or inspiratory obstruction, and timing of the obstruction. Multiple laryngeal visualisations are needed for each level of obstruction to get a detailed overview of the larynx [45] and these findings will help differentiate between respiratory complications that mimic laryngeal obstructions. EILO has been shown to be more prevalent around the supraglottic level of the larynx: 71% compared to 10% of obstruction at the glottic level [39]. The location of the obstruction is important because it leads to a more appropriate treatment that can strengthen the specific location that is causing abnormalities.

Although CLE is the gold standard for diagnosis [44], it may not always be available or it may not cause sufficient psychological stress to elicit symptoms. Although EIB and EILO cannot be accurately differentiated by history alone [46], a thorough evaluation of case history, auscultation to differentiate thoracic *versus* laryngeal source of respiratory noises and spirometry may be combined to consider a likely diagnosis of EILO [33]. Spirometry has some value in EILO diagnosis, as reductions in both forced expiratory volume in 1 s and forced vital capacity may be present [37, 43]. However, the decline in spirometry values



should not be used as a main indicator for EILO due to its low sensitivity [43]. Although differentiating inspiratory stridor from expiratory wheeze can help distinguish EILO from EIB [33], many individuals with EILO do not have inspiratory stridor [43]. Generally, EIB generally is most severe after 5–20 min after exercise while EILO occurs during exercise and generally resolves within 5 min after exercise [33].

## Management

Although the literature contains useful information regarding treatment options for EILO, evidence is limited compared to other airway conditions, such as asthma and EIB. Many of the treatment options for EILO are derived from interventions used for VCD in nonexercise situations. The most common treatment approach has included diaphragmatic breathing control and/or laryngeal exercise performed under the guidance of a speech-language pathologist [41, 47, 48]. During these sessions, that patient is taught the anatomy of their thoracic region and how to visualise their breathing process in attempt to control their symptoms. However, diaphragmatic and vocal fold control can only be effective in certain environments, and may not portray realistic competitive factors that trigger the symptoms. It can be useful for the speech-language pathologist to attend an exercise session to view how the patient becomes symptomatic in a natural environment and attempt to treat the problem in that setting [41]. Further research is necessary to determine how to optimise the efficacy of interventions for EILO. Some athletes have undergone supraglottic surgical intervention [49] in order to strengthen the vocal folds during inspiration while other patients experience laryngeal muscle strengthening and control such as speech therapy, psychotherapy, hypnosis and biofeedback [50]. Respiratory muscle training may also be useful for treating EILO [51] but further research is needed.

## Common nonairway causes of dyspnoea in athletes

While EIB and EILO are common causes of dyspnoea in athletes, general dyspnoea-related terms reported by athletes may be indicative of suboptimal function elsewhere and may not even represent a pathological condition. Indeed, unexplained fatigue with associated dyspnoea is a fairly common presentation in the athletic population and airway dysfunction is only one of many causes of underperformance in athletes [52]. In this section, we present some common reasons of nonairway origin that may impair athletic performance and cause athletes to report a sensation of dyspnoea.

## Iron depletion and deficiency, and anaemia

Iron deficiency and anaemia should be considered in those athletes who report shortness of breath but do not have signs or symptoms of airway disease. Iron deficiency or anaemia may cause the sensation of breathlessness or laboured breathing during exercise, ultimately due to decreased availability of oxygen to the working muscles. Inadequate red blood cell or haemoglobin (Hb) availability or function can lead to tissue hypoxia, which results in various compensatory mechanisms, including increased heart rate and ventilation [53, 54]. Ultimately, this can result in decreased endurance exercise performance, especially at higher intensities, as well as impaired recovery from sprint-interval exercise (*e.g.* football or rugby). If untreated, iron deficiency can ultimately develop into anaemia. Patients with iron-deficiency anaemia typically present with a variety of hypoxia-related physiological symptoms including fatigue, dyspnoea, syncope and cardiac issues related to the increased cardiac output requirements.

The prevalence of iron-deficiency anaemia in athletes is ~3%, which is comparable to the prevalence in the general population [55]. However, this condition may be especially common in endurance athletes [56], who often report decreased performance during exercise. For instance, one study in 45 elite marathoners identified 15 athletes with iron deficiency [57].

## Causes of iron deficiency

Many potential contributors to the development of anaemia in athletes have been identified. Dilutional pseudoanaemia is related to the exercise-induced decrease in Hb concentration that often occurs in endurance athletes [56]. Training causes an increase in both red blood cell count and plasma volume but plasma volume increases at a disproportionately higher rate, creating a net decrease in Hb concentration. Foot impact is the main cause of haemolysis in athletes who participate in high-volume foot-strike activities. Intravascular haemolysis may also occur through oxidative damage, membrane damage related to osmotic homeostasis or compression of muscle groups on capillaries [58]. The incidence of haemolysis is correlated to the intensity of acute exercise [55]. Iron insufficiency can also be a result of nutritional deficits. Iron loss in athletes is typically associated with gastrointestinal bleeding, haematuria, sweating, and menstrual blood loss in women [55, 59].

## Diagnosis of iron deficiency

Conflicting opinions abound regarding the proper diagnostic parameters for iron-related issues and anaemia in athletes. The clinician must be able

to discriminate between iron-deficiency anaemia and other causes of anaemia. Many different blood biomarkers have been used to diagnose anaemia including Hb concentration, haematocrit, iron, ferritin, soluble transferrin receptor (sTfR) and total haemoglobin (tHb) mass [60]. It is generally agreed that to properly diagnose anaemia, a diagnostic test of multiple parameters should be utilised, as opposed to a simple iron or Hb test, and diagnostic algorithms are available [60]. The terminology for iron-related deficiencies is not especially standardised and diagnostic thresholds are not consistent. An example classification scheme was provided by PEELING *et al.* [61], who described the following three levels of iron deficiency and anaemia:

- iron depletion (serum ferritin  $<35 \mu\text{g}\cdot\text{L}^{-1}$ , Hb  $>115 \text{g}\cdot\text{L}^{-1}$  and transferrin saturation  $>16\%$ );
- deficient erythropoiesis (serum ferritin  $<20 \mu\text{g}\cdot\text{L}^{-1}$ , Hb  $>115 \text{g}\cdot\text{L}^{-1}$  and transferrin saturation  $<16\%$ ); and
- iron-deficiency anaemia (serum ferritin  $<12 \mu\text{g}\cdot\text{L}^{-1}$ , Hb  $<115 \text{g}\cdot\text{L}^{-1}$  and transferrin saturation  $<16\%$ ).

Other studies have used slightly different cut points but serum ferritin levels  $<40 \mu\text{g}\cdot\text{L}^{-1}$  are generally the threshold for concern.

The standard tests of iron status are often influenced by inflammation, especially in an athletic population. sTfR may be a better measure due to its low biological variability and stability following exercise stimulus. sTfR/log(ferritin) (sTfR index) has been shown to provide an elevated diagnostic value in detecting iron deficient anaemia as well as differentiating between iron deficiency anaemia and anaemia of chronic disease [62]. Total Hb mass, as measured using a carbon monoxide rebreathing technique, reflects the red cell mass and Hb concentration, and is emerging as potential novel method for evaluating the oxygen carrying capacity of the blood in athletes with iron deficiency. However, some studies have questioned the sensitivity of using tHb mass to evaluate responsiveness to iron-related interventions [63, 64], whereas others have found it clinically useful [64], suggesting further research is necessary.

### Treatment of iron issues

There are differing opinions regarding the best treatment options for iron-deficient athletes, with oral iron supplementation serving as the classic treatment to increase biomarkers of iron storage [65]. Some studies have shown moderate increases in athletic performance of nonanaemic iron-deficient individuals, while others suggest that nondeficient athletes do not benefit from iron supplementation [66]. One recent meta-analysis revealed anaemic and nonanaemic women with iron deficiency may have an increase in submaximal and maximal aerobic performance through iron

supplementation [67]. Clinicians should use laboratory testing to confirm that iron supplementation is actually necessary, as increased iron stores have been associated with gastrointestinal distress, liver malignoma and impaired immune effector functions [56]. Intramuscular and intravascular iron injections have not provided definitive positive outcomes on athletic performance, but in some cases have improved perceived fatigue levels in nondeficient athletes [64]. PEELING *et al.* [61] and BLEE *et al.* [68] found that intramuscular iron injections improved serum ferritin levels but did not increase exercise performance in iron-depleted athletes.

Dietary modification is commonly recommended for athletes with iron deficiency issues, and is an important component of treatment, but is not sufficient itself to address iron deficiency [60]. One common dietary recommendation is increased intake of haem iron, which is found in meat and generally better absorbed than free iron found in vegetables. It must be noted that vegans are not necessarily at greater risk of iron deficiency than omnivores, and may receive adequate iron in their diet [69]. Although vegan diets are not inherently low in iron, ferritin levels may be somewhat reduced compared to omnivores, but the clinical consequences of this are generally unknown. While this may not be an issue for the general vegan population, it is possible that vegetarian or vegan endurance athletes, who have greater iron turnover and thus dietary needs, may be at greater risk of iron deficiency [69]. However, this is not a well-researched area, and one recent systematic review identified no differences in performance between athletes consuming vegetarian *versus* omnivorous diets [70].

### Infectious disease

A number of infectious diseases may cause athletes to underperform and feel fatigued [52], which may ultimately cause an athlete to present with dyspnoea-related complaints. Generally, athletes suffering with infectious disease will also report general malaise, tiredness, unusual musculoskeletal soreness, and have other signs or symptoms well beyond those seen with airway diseases and iron deficiency. Athletes may continue to train and compete at suboptimal levels for some time before it is realised that infectious disease is at the root of their symptoms. As such, it is important for clinicians to be vigilant about the possibility of infectious disease in athletes reporting shortness of breath, especially when accompanied by other signs and symptoms. Because an exhaustive list of the numerous infectious diseases, including insect- and tick-borne pathogens, that may cause underperformance that results in complaints of underperformance (and associated dyspnoea) [71] is

## Self-assessment questions

- 1) An athlete with EIB without other comorbidities is most likely to have:
  - a. Difficulty breathing at the start of exercise
  - b. An inspiratory stridor that is most severe during exercise
  - c. An expiratory wheeze that is most severe after exercise
  - d. Sharp pain during inspiration
  - e. Sharp pain during expiration
- 2) Athletes with EILO:
  - a. Always have an inspiratory stridor
  - b. Have EIB as a comorbidity about one-third to one-half of the time
  - c. Commonly experience pain during expiration
  - d. Favourably respond to asthma medications, even if they do not have EIB
  - e. Usually have symptoms of laryngeal dysfunction at rest also
- 3) An 18-year-old, female soccer player presents with a chief complaint of shortness of breath and chest tightness during and after exercise. Which of the following is the most appropriate plan of action?
  - a. She should be treated with a bronchodilator inhaler for at least 1 month to see if her symptoms improve.
  - b. She should try increasing dietary iron or potentially take an iron supplement for 3 months to see if her symptoms improve.
  - c. She should consult with a qualified personal trainer or strength and conditioning coach to attempt to improve her aerobic fitness within the next 6 months.
  - d. She should not change anything and see if the symptoms resolve themselves in the next 1–2 months.
  - e. A detailed patient history, including targeted exercise and symptom-specific questions, should be undertaken to determine the appropriate diagnostic protocol.
- 4) A 22-year-old, male university lacrosse player presents with a 1-week-long history of dyspnoea during team practices. Which of the following would be the most valuable initial step in the clinical work-up?
  - a. Referral to a pulmonologist for asthma/EIB evaluation
  - b. Through case history and physical exam, including indicators of thoracic trauma
  - c. Complete blood count/chemistry with iron status evaluation
  - d. Referral to exercise physiologist for  $\dot{V}O_{2\max}$  test
  - e. Referral to otorhinolaryngologist for EILO evaluation, including continuous laryngeal endoscopy
- 5) A 21-year-old, male distance runner presents complaining of dyspnoea. Another healthcare provider has suggested he has EIB but regular use of his bronchodilator inhaler for the past month has not fully resolved the issue. Which of the following could realistically account his poor response to treatment?
  - a. He does not actually have EIB and therefore the bronchodilator is not effective to address the cause of his dyspnoea
  - b. He does have EIB but is not using his bronchodilator correctly
  - c. He does have EIB but also has a comorbidity that remains untreated
  - d. He does have EIB but is not responding ideally to correct use of the current bronchodilator therapy
  - e. All of the above are realistically possible

beyond the scope of this article, we will focus on one common disease in high school and collegiate athletes.

## Epstein-Barr virus/infectious mononucleosis

Infectious mononucleosis, caused by the Epstein-Barr virus (EBV), is especially common in adolescent and young adult athletes, with a peak incidence in the 15–24-year-old age group, but becomes nearly negligible after 35 years of age [72]. EBV viral loads may be higher and antibody titres lower in athletes [73]. Mononucleosis may include a number of signs, including pharyngitis, lymphadenopathy and rash. In addition to the general fatigue caused by the virus, dyspnoea may occur as a result of the pharyngitis itself [74]. However, athletes may present without these classic signs and only complain of symptoms related to exercise performance [72], which may make it difficult to initially differentiate from overtraining syndrome. As such, laboratory testing for mononucleosis should be included for young athletes who present with complaints of impaired performance. However, during the initial 3 weeks of infection, there is a high likelihood of false negative results on heterophile antibody titres [72]. Viral capsid antigen tests may be used in the event that mononucleosis is suspected but antibody titres are negative [72]. However, it should also be noted that EBV early antigen antibodies remain elevated throughout the year and therefore the presence of antibodies alone is not sufficient for diagnosis [75]. Other viral and bacterial pathogens may also cause similar symptoms.

## Other diseases

The conditions referred to in this article are relatively common in athletes and may be frequently seen in general clinical practice. However, this is not meant to be an exhaustive guide, as a number of other conditions may present as dyspnoea, as indicated by case reports of psychogenic causes [76], congenital heart anomalies [77], myocarditis [78] and various other pathologies. It is indeed possible that significant and dangerous cardiovascular and pulmonary diseases may exist and initially cause an active individual to present with dyspnoea during exercise. As such, a thorough physical examination is necessary to check for the presence of abnormal heart and lung sounds, and other signs of systemic disease. Likewise, indications of potentially more concerning conditions, such as syncope or dysrhythmia, should be referred for specialist examination. Furthermore, follow-up visits after diagnosis and initiation of treatment should serve as standard practice to verify a positive response to treatment and ensure that further diagnostic testing is not necessary.

## Musculoskeletal causes of dyspnoea

Musculoskeletal disorders are a rare source of dyspnoea in the general population, though the physical demands of certain sports can cause injury or exacerbate anatomic deformities, which can ultimately lead to dyspnoea in athletes. Musculoskeletal sources of dyspnoea can be grouped into two general categories: 1) pain-causing dysfunction of the ribs and spine; and 2) deformation of the thoracic cage.

### Pain-causing dysfunction of the ribs and spine

Rib dysfunction can present obviously as contused or fractured ribs. Less obvious injuries are stress fractures in sports like golf [79] and rowing [80], and dysfunction at the interface of the ribs with the spine at the costotransverse or costovertebral joints. Rib contusion/fracture is a common chest injury, especially after trauma as in a motor vehicle accident [81, 82] or in a collision sport like American football [83, 84]. The commonality for traumatic rib fractures, stress fractures and rib joint dysfunction is pain causing distressed breathing and dyspnoea. Recent research has shown that dyspnoea, like pain, has both a sensory (intensity) and affective (immediate unpleasantness followed by higher order interpretations of suffering) domain [85–88]. Pain may be more harmful than the actual loss of bone integrity since the pain limits breathing, reduces functional residual capacity and may lead to atelectasis [89]. Other forms of sports-related trauma can cause dyspnoea due to conditions such as pneumomediastinum [90] and pneumothorax [91], and must also be considered following trauma.

While the onset of a rib fracture from trauma has a quite obvious history, less obvious are stress fractures and dysfunction of the costovertebral and costotransverse joints. Stress fractures of the ribs are thought to be caused by tensile and rotational stress of a repetitive nature [92]. The athlete will frequently report either an unknown onset (upon further questioning, the examiner will discover a recent excessive volume of training), or that the athlete took a hard swing, felt sharp pain and was unable to continue. Physical examination often reveals pain over the posterolateral aspect of ribs 4–9 [79, 80]. Treatment recommendations for rib stress fractures in athletes come mostly from case studies or case series and has not progressed much in 20 years. General recommendations are to cease the offending activity for 4–6 weeks and then slowly return to sport using pain as a guide, with a focus on changing and (hopefully) improving technique [92].

Still painful, but to a lesser extent, is dysfunction of the costovertebral and costotransverse joints.

As with a stress fracture of the ribs, the athlete may report onset of pain after rapid or repeated twisting, or be unable to identify an inciting event at all. Both of these joints are well innervated by branches of the intercostal nerve, meaning that dysfunction can cause pain, especially with palpation. This pain is predominantly local and felt as a deep, dull ache [93]. This injury can be differentiated from a rib stress fracture by pain with palpation over these joints. Research literature provides little to no guidance on treatment of these joints. Clinically, in more than 25 years of practice, we have found great success in an approach using manipulation and mobilisation including mobilisation with movement. Some support for this approach comes from improved understanding of the neurophysiological mechanisms by which manual therapy affects a decrease in pain [94].

Pain outside the thoracic cage, specifically in the cervical spine, has been proposed as a source of dyspnoea [95, 96]. Kapreli and co-workers [96–98] propose that in chronic neck pain, the patient develops a forward head posture, and the deep neck flexors and extensors become weak causing substitution and hyperactivity of the superficial cervical musculature, specifically, the sternocleidomastoid, upper trapezius and anterior scalene muscles. The theory is that these factors, along with pain and kinesiophobia, may predispose patients with chronic neck pain to respiratory dysfunction, like decreased maximal inspiratory and maximal expiratory pressure. It is important to note that these studies were not performed in athletes. Also important for clinicians working with athletes with both neck pain and dyspnoea is that in addition to dyspnoea being a psychophysiological sensation like pain, one common treatment for neck pain, manipulation of the cervical spine, has been reported to be a pathophysiological source of dyspnoea. The phrenic nerve, which innervates the diaphragm, has its origin from the C3–C5 nerve roots. While likely a rare occurrence, multiple case reports exist demonstrating unilateral or bilateral diaphragmatic paralysis after chiropractic manipulation [99–102].

### Deformation of the thoracic cage

In addition to association with painful dysfunction of the ribs and spine, dyspnoea has also been associated with deformation of the thoracic cage. The most common deformation is scoliosis, with a prevalence estimated between 5% and 9%, with decreasing prevalence as the definition of scoliosis changes from  $\geq 10^\circ$  to  $\geq 40^\circ$  [103, 104]. Patients with more severe curves are more likely to experience dyspnoea [105] but with vigorous exercise, even those with mild to moderate scoliosis are likely to experience decreased pulmonary function [106]. In addition, some 32% of patients will have back pain associated with their scoliosis [107], which might contribute to dyspnoea in

## Suggested answers

- 1) c
- 2) b
- 3) e
- 4) b
- 5) e

an athlete. Conservative treatment of scoliosis for years has been approached from a bracing and corrective exercise approach with regard to the still-developing adolescent. While there is now some evidence to support this approach [108–110], many of the athletes we see are mature and dealing with the episodic pain/dysfunction that comes from strenuous exercise at a highly competitive level with less than optimal thoracic cage structure and mobility. In these athletes, the focus of treatment tends to be on pain-relieving manual therapy techniques and mobility with adjunctive pain-relieving modalities, as needed.

While the deformity in scoliosis is predominantly in the frontal plane, hyperkyphosis is predominantly in the sagittal plane and affects the thoracic spine. Hyperkyphosis is most often associated with increasing age and has been found to be associated with dyspnoea. In a study of 130 older kyphotic patients, 40% had an adjusted prevalence odds ratio of 2.5 for dyspnoea [111]. Although generally associated with age, certain sports may be associated with increased thoracic kyphosis and, therefore, may predispose the athlete to dyspnoea. Women's field hockey players may have a relatively higher prevalence of kyphosis [112] as do adolescent athletes in general [113]. Athlete-related hyperkyphosis is thought to be related to biomechanical factors related to load during training. Load, along with genetic predisposition, may be a factor in idiopathic hyperkyphosis or Scheuermann's disease [114]. Both pain and dyspnoea are symptoms associated with this deformity, and probably hyperkyphosis in general due to altered respiratory mechanics [115]. Treatment of Scheuermann's disease in the adolescent, like idiopathic scoliosis, involves bracing and exercise (strengthen extensor groups and stretch flexor groups). Although this approach is the current clinical norm, there is little or no research to support or refute this approach [116].

## Inadequate fitness and physiological limitations

It is common for individuals of poor or excellent aerobic fitness to complain of dyspnoea during exercise without any evidence of pathology. A representative example of this is seen in one study of 142 athletes with a complaint of exercise-induced dyspnoea, in which 74 (52%) individuals did not have any pathology, and of those, 48 had normal to good aerobic fitness and 26 had poor aerobic fitness [117]. Otherwise healthy athletes with poor fitness may report dyspnoea due to being unaccustomed to the ventilatory demands of unfamiliar exercise, have a preconceived notion of their fitness level based on previous experience, or may have to exert more effort to keep up with their more fit counterparts in a team environment. It is also possible for athletes to experience overtraining syndrome, which is characterised by otherwise

unexplained decreased performance [118, 119], which may result in dyspnoeic symptoms.

Although gas exchange is generally not a barrier to aerobic performance in healthy individuals, highly trained endurance athletes may have such extensive cardiovascular, neuromuscular and metabolic adaptations that they cannot fully oxygenate blood as it passes through the pulmonary microcirculation at high cardiac outputs [120]. Highly trained athletes may experience an expiratory flow limitation [121], such that they achieve their ventilatory limits [122]. It is possible that expiratory flow limitation could be overcome through controlled breathing methods or respiratory muscle training, but specific interventions to overcome flow-limited athletes is lacking. Approximately half of healthy elite endurance athletes may experience exercise-induced arterial hypoxaemia [123] due to nonpathological anatomical or physiological shunting of blood within the cardiopulmonary system, including ventilation-perfusion mismatching [124]. All of these mechanisms can ultimately cause highly trained healthy athletes to report a sensation of dyspnoea.

## Exercise testing considerations for dyspnoeic athletes

Exercise testing, including measurement of maximal oxygen uptake ( $\dot{V}O_{2\max}$ ), is commonly performed in laboratory settings to quantify aerobic performance, and may sometimes be ordered for the evaluation of dyspnoeic or underperforming athletes. It must be emphasised that exercise testing should be replicate the type and intensity of exercise in which symptoms take place. Multiple exercise testing procedures may be performed simultaneously to maximise efficiency (*i.e.* combination of dry-air  $\dot{V}O_{2\max}$  testing with pre- and post-exercise spirometry, pulse oximetry, continuous laryngeal endoscopy, ECG/echocardiography, *etc.*). Spirometry during exercise may be used to determine whether an expiratory flow limitation exists [122]. Although the recommended threshold varies, pulse oximetry values <92% are indicative of hypoxaemia. However, other case details must be used to differentiate between pathological *versus* nonpathological causes of hypoxaemia.

Although  $\dot{V}O_{2\max}$  testing is useful for examining athletic performance, its diagnostic value in evaluating dyspnoeic athletes has some limitations, especially if pre-symptomatic baseline are not available. Athletes who experience symptoms of dyspnoea severe enough to stop exercising prematurely will not attain a true physiologic  $\dot{V}O_{2\max}$  (*i.e.* the test is not limited by their cardiometabolic fitness). Endurance-trained athletes, as well as those who engage in sprint-interval based sports, are expected to have high  $\dot{V}O_{2\max}$  values, such that

their  $\dot{V}O_{2\max}$  may be well above average even in the presence of conditions that negatively influence their performance. Likewise, athletes in nonendurance sports do not necessarily have high  $\dot{V}O_{2\max}$  values, and therefore only unusually low  $\dot{V}O_{2\max}$  values would be expected to provide novel information other than confirming inadequate fitness.

## Conclusions

Dyspnoea, fatigue and underperformance are often interrelated symptoms in athletes, and may have various causes, ranging from benign

to potentially deadly. While airway conditions, namely asthma and EIB, are often at the top of the differential diagnosis list, numerous other conditions must also be considered. To avoid frustration and catastrophic mistakes, it is essential for clinicians to obtain a thorough patient history, including detailed exercise-specific questions, and then develop and conduct an appropriate diagnostic plan. Following implementation of a proper management plan for the identified diagnosis, clinicians should regularly follow up with patients to ensure that the intervention is working, as comorbidities and nonadherence to treatment recommendations can negatively influence outcomes.

## Conflict of interest

None declared.

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