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Dyspneic athlete

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Abstract Breathing concerns in athletes are common and can be due to a wide variety of pathology. The most common etiologies are exercise-induced bronchoconstriction (EIB) and paradoxic vocal fold movement disorder (PVFMD). Although some patients may have both, PVFMD is often misdiagnosed as EIB, which can lead to unnecessary treatment. The history and physical exam are important to rule out life threatening pulmonary and cardiac causes as well as common conditions such as gastroesophageal reflux disease, sinusitis, and allergic etiologies. The history and physical exam have been shown to be not as vital in diagnosing EIB and PVFMD. Improvement in diagnostic testing with office base spirometry, bronchoprovocation testing, eucapnic voluntary hyperpnea (EVH) and video laryngoscopy are essential in properly diagnosing these conditions. Accurate diagnosis leads to proper management, which is essential to avoid unnecessary testing and save healthcare costs. Also important to the physician treating dyspnea in athletes is knowing regulations on medications, drug testing, and proper documentation needed for certain organizations. The differential diagnosis of dyspnea is broad and is not limited to EIB and PVFMD. Ruling out life threatening cardiac and pulmonary causes with a proper history, physical, and appropriate testing is essential. The purpose of this review is to highlight recent literature on the diagnosis and management of EIB and PVFMD as well as discuss other potential causes for dyspnea in the athlete.

Keywords Exercise induced bronchoconstriction · Vocal cord dysfunction · Paradoxic vocal fold movement disorder

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Introduction

Exercise induced bronchoconstriction (EIB) describes acute, transient airway narrowing that is provoked by exercise. EIB is characterized by cough, expiratory wheezing, shortness of breath, fatigue, and/or chest tightness brought on by exercise [1••]. EIB refers to patients who have no symptoms outside of exercise where exercise induced asthma (EIA) is defined as the transitory increase in airway resistance that typically occurs following vigorous exercise in a patient with chronic asthma [2]. Some patients with asthma will only have symptoms with exercise, so confirming that no symptoms or decrease in pulmonary function occur at rest is paramount in guiding treatment [3]. Anywhere from 80 %–90 % of patients with chronic EIA and 10 %–40 % of patients with allergic rhinitis and atopic dermatitis will have EIB [4–6].

Vocal cord dysfunction (VCD) has been described with other terminology including PVFMD. A shift away from the term "vocal cord dysfunction" has occurred primarily because of confusion with pathologic abnormalities causing dysphonia rather than dyspnea. The distinction between PVFMD and pathologic conditions causing paresis or paralysis is important as patients with PVFMD do not have any permanent deficit in vocal cord mobility [7••]. This disorder occurs when someone with normal vocal fold motion suffers from intermittent narrowing of the vocal folds during respiration [7••]. It can be characterized by the intermittent, abnormal paradoxical adduction of the true vocal cords during respiration resulting in variable upper airway obstruction. Patients with PVFMD usually present with intermittent shortness of breath of varying intensity, inspiratory stridor, choking, throat tightness, voice changes, or cough. All of these symptoms often resolve shortly after relaxation or cessation of activity [8•], which differs from the symptomatology of EIB, which may worsen.

EIB

Epidemiology

EIB is more common in athletes than the general population and is seen across all athletic settings, however, its prevalence varies due to differences in testing methods, thresholds for diagnosis, and participant participation [1••, 9]. EIB is prevalent in endurance as well as cold weather and winter sports likely due to environmental exposure in addition to higher ventilatory demands [10–12].

Other environmental triggers include chlorine in swimming pools [13, 14] chemicals from resurfacing ice hockey rinks [15], and in urban areas from automobile exhaust [16]. EIB may be underestimated as athletes have been shown to be poor perceivers of bronchospasm [17, 18] and lack awareness of symptoms [19, 20]. Also athletes underreport symptoms in fear of losing playing time [21].

Pathophysiology

The pathophysiology of EIB is not completely understood and different theories are still debated. The water loss theory attributes EIB to the loss of water through the bronchial mucosa as the body tries to rapidly warm inhaled air during exercise. Local dryness and other factors are thought to trigger bronchoconstriction [22]. Another theory is thought that EIB is due to respiratory heat loss from increased ventilation, which as a result causes airway cooling. Symptoms can continue once exercise is stopped as blood vessels dilate and engorge to rewarm the epithelium, which may lead to rebound hyperemia and bronchoconstriction [23]. Other studies have demonstrated that the presence of inflammatory mediators is involved in EIB [4, 24, 25].

Presentation

Clinical manifestations are variable and range from complaints of poor performance to severe bronchospasm and respiratory failure [9]. Shortness of breath starts at least 5–10 minutes into exercise as workloads of at least 80 % maximum oxygen consumption for 5–8 minutes are required to induce EIB [9]. If patients exhibit symptoms sooner than this EIB is less likely and other diagnosis such as PVFMD should be considered [9]. Symptoms may be still be apparent after exercise is completed and remain significant for 30 minutes and even up to several hours or longer if no bronchodilator is used.

The presence of EIB can be challenging clinically because symptoms can be nonspecific and other medical conditions can present with overlapping symptomatology. The diagnosis of EIB based on history and self-reported symptoms alone are often unreliable and can both under diagnose as well as over diagnose the condition [26–28]. Starting with the history and physical examination is appropriate in every patient. When considering EIB, it is essential to rule out other problems that mimic EIB such as, but not limited to; cardiac causes, PVFMD, dysfunctional breathing, and reflux [1••].

Testing

When symptoms are mild, and more life threatening causes have been ruled out, some physicians start with a trial of a short acting beta agonist like albuterol. This is not recommended as improper diagnosis can lead to inappropriate treatment. Objective testing should begin with spirometry before and after bronchodilator therapy [1••] as this will assist in diagnosing patients with impaired lung function at rest such as asthma, COPD, or other pulmonary problems. As its name implies, most people with EIB have normal lung function at rest [29] so bronchoprovocation testing is usually warranted. There are several different types of bronchoprovocation tests, each with their limitations. The International Olympic Committee (IOC) does require eucapnic voluntary hyperventilation (EVH) testing for documenting EIB in athletes. This involves hyperventilation of a mixture of 5 % CO2 and 21 % O2 at a ventilation rate of 85 % of the patient's maximal voluntary ventilation in 1 minute (MVV). The patient hyperventilates for 6 minutes and interval FEV1 measurements occur for up to 20 minutes after hyperventilation is completed. A drop in the FEV1 of at least 20 % is diagnostic of EIB [10]. EVH has been shown to be highly specific [30] and more sensitive than methacholine [10], lab, and field testing [30]. In addition, it is the preferred method of diagnosing EIB in patients who exercise regularly but who are considered nonathletes [31•].

Treadmill testing in pulmonary function testing laboratories is the most available and widely utilized. If EVH is not available, this is the next best test. The optimal test is 8 minutes in duration and allows the patient to reach 80 %–90 % of their maximal heart rate by 2 minutes into the test and maintain it for the following 6 minutes [32, 33]. False negative results may occur if adequate exercise and environmental stress are not provided in the evaluation of EIB [1••]. A decrease of 10 % in FEV1 (forced expiratory volume at 1 second) between pre- and post-testing is diagnostic of EIB [34].

Mannitol bronchoprovocation is a newer form of osmotic airway testing that uses increased inhaled doses of mannitol while subsequently measuring FEV1. It is a portable form of testing and has been shown to correlate well with exercise testing and EVH [35]. Mannitol inhalation can cause cough, which may lead to lower mannitol deposition in the lungs and false negative results [36].

Field testing is less sensitive than EVH and lacks standardization and involves athletes having pre- and postlung function testing while performing their sport [37]. Methacholine

testing has also been shown to be less sensitive than EVH and is not recommended as first line testing [38•].

In a patient with persistent symptoms, negative spirometry and bronchoprovocation tests an alternate diagnosis should be considered [1••].

Treatment

The most common treatment is with 2 puffs of a short acting beta agonist (SABA) such as albuterol 15–30 minutes prior to exercise, which will provide peak bronchodilation in 15–60 minutes and protect from EIB for at least 3 hours [39]. As frequent use of SABAs may lead to tachyphylaxis, the addition of a controller medication such as an inhaled corticosteroid is recommended when SABAs are used daily or more frequently [38•]. Corticosteroids are not intended for acute control and may take anywhere from 2 to 4 weeks to have an effect. They are considered first-line in patients who have chronic asthma in addition to EIB [39].

Long acting beta agonists (LABA) are not recommended for single therapy in asthma or EIB due to risk of tachyphylaxis and serious side effects [38•, 40]. Leukotriene modifiers such as montelukast are effective in treating EIB when given daily or 2 hours prior to exercise [41]. There has been no development of tolerance when leukotriene modifiers are given daily [42]. Mast cell stabilizers and cromolyn compounds are effective but mainly used second-line because of cost, lack of availability, and their decreased efficacy and duration of action compared with SABA [1••].

A pre-exercise warm up in some patients can lead to a refractory period for about 2 hours after this warm-up session and can lead to less symptoms of EIB [43, 44], however, it is tough to predict who will experience this [45]. Other options include nose breathing and/or wearing a mask or scarf to help warm and humidify the air. This has been shown to be valuable in winter sport athletes [46]. Other options, which have been tested in small studies but not validated in larger studies, include salt restricted diets, fish oil, and vitamin C [47–49].

PVFMD

Epidemiology

PVFMD is likely underdiagnosed and this has been shown to lead to increased health care costs [50–52]. The prevalence is unknown as there are no large, prospective, population based studies [53]. An estimated 2 % to 3 % of the general population is affected [54] and some studies suggest that PVFMD occurs in up to 27 % of patients referred for EIB [55]. The overall prevalence of PVFMD in developmental and elite athletes is estimated to be 5.1 %, and, interestingly, the outdoor athlete group had a higher prevalence of 8.3 % compared with 2.5 % found in the indoor group [54]. It has been proposed that PVFMD is seen more commonly in sports requiring short high bursts of ventilation, such as sprinting, cycling, and ice hockey [8•]. It has also been shown to be more common females than males [54, 56]. The proposed mechanism is that these higher ventilation bursts require breathing more through the mouth, resulting in cooler and drier air than can irritate the vocal cords [8•]. PVFMD has been found to be present at rates of up to 40 % among patients with refractory or exercise-induced dyspnea [50, 57–59]. Exercise-associated PVFMD accounts for approximately 14 % of PVFMD diagnoses [60•]. It occurs predominantly in young female athletes who present with dyspnea and sometimes stridor triggered by exercise [60•]. In a series of 831 patients with PVFMD, 46 were elite athletes and of these, 70 % were female and 46 % were noted to have noisy breathing during exercise [60•]. Elite athletes with PVFM were less likely to have a history of reflux, psychiatric diagnosis, dysphonia, cough, or dysphagia, compared with non-athletes who had PVFMD [60•].

Pathophysiology

The underlying pathophysiology of PVFMD was originally thought to be primarily psychological for years, with stress and anxiety being the primary triggers [61]. Currently, the cause is thought to vary from patient to patient, depending on which comorbidities are present. Irritant receptors are thought to play a role in airway protection [62] and PVFMD represents a hyperfunctional glottis closure reflex induced by repetitive irritants [63]. Husein and colleagues established in 2008 that 70 % of their patients had symptoms consistent with mental illness. However, 50 % of their patients had comorbid conditions such as gastroesophageal reflux disease or asthma, and they were more likely to have these medical conditions than they were to have a psychiatric history [64]. Stress and anxiety are still linked to triggering PVFMD, but anything that irritates the vocal folds can make paradoxical movement more likely [61]. Tobacco, allergic laryngitis and rhinosinusitis, viral illness, and untreated sleep apnea are other factors that can lead to PFVMD [65, 66]. Laryngeal edema, associated with reflux complaints in 90 % of patients, was found in 72 % of patients diagnosed with PFVMD [61]. PVFMD may represent a subset of the irritable larynx syndrome, described by Morrison and colleagues in 1999 [67].

Presentation

Patients who eventually get diagnosed with PVFMD usually have a presentation that often mimics asthma, although it can occur with asthma or other pulmonary disease [7••]. Shortness of breath usually comes on quicker in PVFMD than in asthma

and also resolves faster with rest [7••, 54]. Athletes with PVFMD usually complain of more inspiratory symptoms rather than expiratory symptoms. These symptoms include noising breathing, inspiratory stridor, or a choking sensation [68]. Several studies have linked reflux disease to PVFMD [69, 70]; however, it is important to note that gastroesophageal reflux disease and laryngopharyngeal reflux can exist without symptoms [71]. In acute presentations, patients with PVFMD have normal blood oxygenation levels and no cyanosis [72].

Testing

Pulmonary function tests (PFTs) are usually done prior patients being referred for laryngoscopy [7••]. PFTs can be normal or have inspiratory limb flattening on flow volume loop or increased symptoms after methacholine challenge without a response to bronchodilators. PFTs are important as coexisting pulmonary disease can occur in addition to PVFMD. However, the presence of positive PFTs should not stop the clinician from further investigation with laryngoscopy if PVFMD is suspected [7••]. Physical exam findings are inconsistent in diagnosing PVFMD and flexible laryngoscopy is needed to visualize vocal fold movement to aid in the diagnosis [7••]. Patients with PVFMD show narrowing (adduction) of the vocal cords with both inspiration and expiration, however, there is more marked narrowing on exhalation [54, 73, 74]. Laryngoscopy can visualize vocal cord movement during regular breathing as well as provocative behaviors (Valsalva, odors, exercising) and then assess corrected motion after therapeutic breathing techniques have been demonstrated [7••]. It is important to note that laryngoscopy is essential to rule out other underlying pathologies as coexisting diagnoses has been shown to be as high as 33 % [60•, 69]. If PVFMD is highly likely but not seen on laryngoscopy, athletes suspected of having this should still be treated [7••] if other etiologies such as pulmonary and cardiac causes have been ruled out.

Treatment

Behavioral therapy, referred to as Laryngeal Control Therapy (LCT) with a speech language pathologist experienced with this disorder is essential in treating PVFMD [7••, 8•]. The details of how this is conducted is beyond the scope of this article but is has been shown to be up to 95 % effective [60•, 75]. Patients are encouraged to practice symptom relieving breathing techniques even when asymptomatic to help establish muscle memory, which is thought to help minimize recurrence. Other comorbid conditions that cause hyperresponsiveness of the vocal cords require treatment as appropriate with a multidisciplinary team consisting of but not limited to certified athletic training, pulmonology, otolaryngologist, speech-language pathology, gastroenterology, allergy and immunology, and psychology [8•]. Some of these conditions requiring additional treatment include anxiety, reflux, allergies, sinus disease, dryness, and obstructive sleep apnea. Of note, athletes have lower rates of psychiatric disorders and reflux thus, they may require on-site LCT to help control symptoms [7••]. Other ways patients can control symptoms is with general vocal hygiene and identifying an eliminating individual triggers. Cases of severe PVFMD that cannot be controlled with LCT, the use of benzodiazepines, heliox, or laryngeal botox have shown benefit [76–78].

Other Causes of Dyspnea in the Athlete

Isolated dyspnea from cardiac and other pulmonary causes is not as common as EIB and PVFMD but should still be considered in the differential when evaluating athletes with shortness of breath during exercise. EIB and PVFMD happen more consistently with exercise where the initial presentation of cardiac causes could be sudden cardiac death. Other symptoms include chest pain, dyspnea disproportionate to the exercise performed, palpitations, dizziness, or syncope. Numerous pathologies, which go far beyond the scope of this article, include both congenital and acquired structural and vessel abnormalities as well as rhythm disturbances. Initial work up starts with a history and physical exam beginning with vital signs looking for fever (assessing myocarditis) as well as personal and family history of risk factors (family history of cardiac problems including arrhythmias, early sudden cardiac death, and risk factors for CAD if over age 35). Physical exam should focus on the cardiovascular system and assessing for marfanoid stigmata.

In an athlete with dyspnea and associated chest pain with a concern for cardiac causes, the initial work up usually starts with obtaining an electrocardiogram (EKG/ECG) and blood tests if indicated (troponins if concern for myocarditis or CAD in the masters athlete). If warranted, the EKG is usually then followed with additional testing with Transthoracic Echocardiography (TTE) and/or stress testing. A TTE can show valvular problems as well as structural problems including hypertrophic cardiomyopathy and sometimes anomalous coronary arteries. Further investigations include holtor monitoring, further imaging with cardiac MRI, CTA, electrophysiological studies, and other invasive studies such as angiography. To our knowledge, there is no specific algorithm to follow with chest pain and dyspnea in the athlete as each patient needs to be approached on an individual basis and managed together with a cardiologist.

Other pulmonary causes of dyspnea in the athlete to consider, although uncommon, include pulmonary embolus (PE) and pneumomediastinum. There have been several cases published recently on pulmonary embolus diagnosed in the athlete [79, 80]. Presenting symptoms include but are not limited to

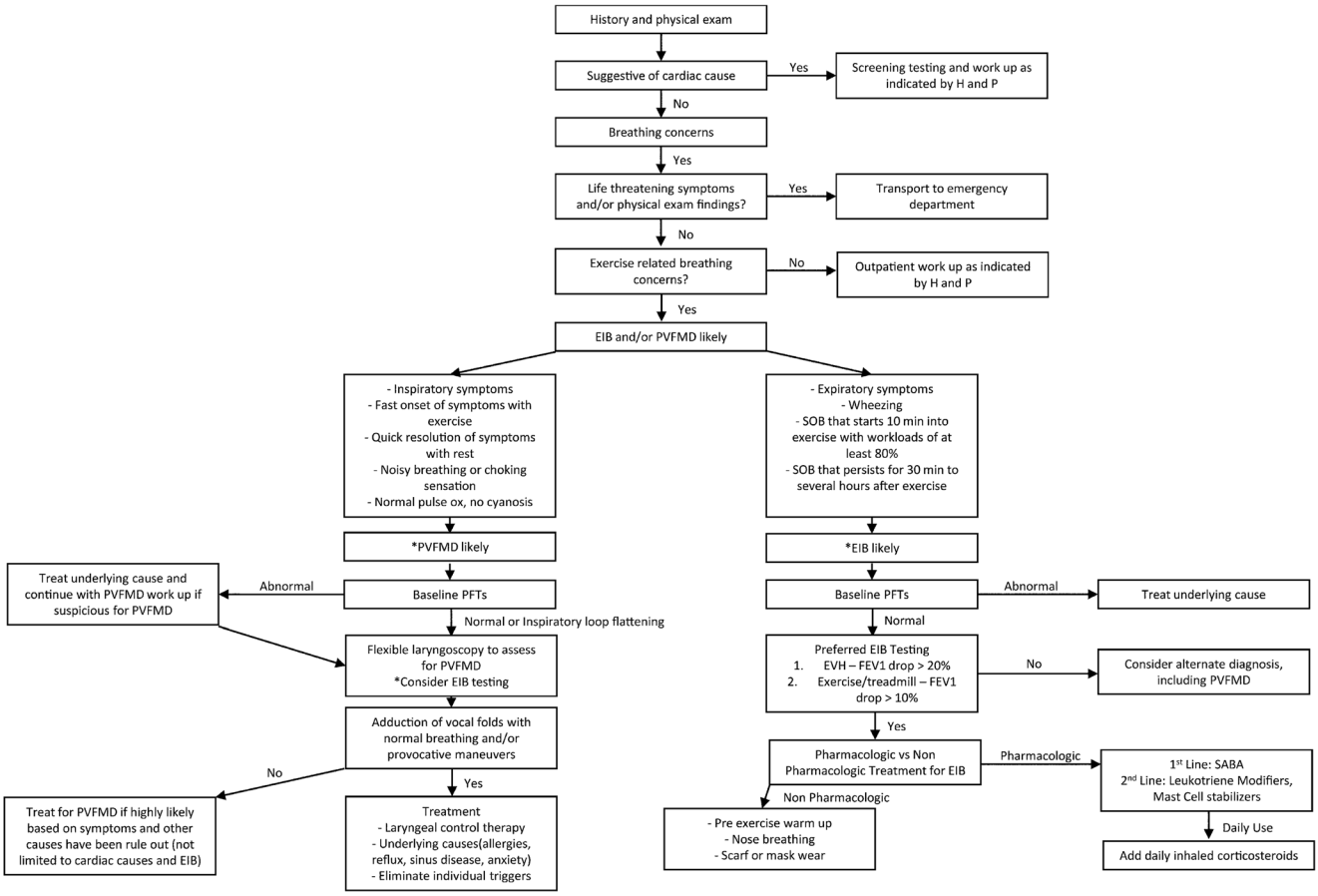

Fig. 1 Suggested algorithm for evaluation and treatment of dyspnea in the athlete. *Indicates that EIB and PVFMD can occur independent of one another or concomitantly and having one does not exclude the other

shortness of breath, chest pain, tachycardia, pleuritic chest pain, and unilateral leg pain/swelling. Accurate diagnosis is essential and begins with considering PE in the differential diagnosis. Risk factor assessment is the same in the athlete and includes personal and family history of clotting disorders, long travel (plane or car rides), use of hormonal contraceptives, and smoking. The validated Wells criteria can help to determine if further tests are needed to assess for PE [81, 82]. This criteria may not encompass the pediatric athlete as demonstrated in a case series [79]. If confirmed, first-time patients with PE are treated by discontinuing hormonal contraceptives if indicated and usually given 3–6 months of daily anticoagulation. Return to play is based on the sport and their risk for trauma that can result in prolonged bleeding. As most athletes are at risk for injury in any given sport, avoidance of sport is usually recommended during anticoagulation.

Pneumomediastinum, although a rare cause of dyspnea in the athlete is another diagnosis to be aware of and there are several case reports documented in the sports literature [83–86]. The most common cause of spontaneous pneumomediastinum is alveolar rupture into the bronchovascular sheath as a result of increased intrathoracic pressure [86]. Symptoms include shortness of breath, chest pain, and radiation of pain into the neck. Diagnosis usually includes a chest X-ray with or without CT scan. Treatment is supportive and at this time there are no clear evidence based return to play guidelines.

Other systemic conditions that can cause dyspnea include but not limited to poor conditioning, overtraining syndrome, exercise induced urticarial/anaphylaxis, and viral illnesses such as infectious mononucleosis are beyond the scope of this article.

Conclusions

A thorough history and physical exam is the starting point for all dyspneic athletes as various pulmonary, cardiac etiologies, and life-threatening causes need to be ruled out. EIB and PVFMD are more common reasons for dyspnea among athletes; however, athletes usually under-report their symptoms. In regards to EIB, diagnosis based on symptoms alone can be inaccurate. Objective testing is key and knowing indications and limitations of each is important. EVH is considered the bronchoprovocation test of choice but is not available in most places. Exercise spirometry is considered second line as long as the exercise is vigorous enough. Both pharmacologic and nonpharmacologic treatments can be effective with first-line

management being the use of SABAs like albuterol 15–30 minutes prior to exercise. If SABAs are used daily, the use of a daily inhaled corticosteroid is recommended for maintenance. The daily use of SABAs or the single use of LABAs is not recommended because of the risk of tachyphylaxis.

There is need for increased awareness of PVFMD as a common cause of respiratory complaints in recreational and competitive athletes, either as a single diagnosis or in combination with EIB. The onset of dyspnea in PVFMD is usually much sooner during exercise than in asthma and also resolves faster with rest. Patients usually undergo PFTs, which may be abnormal; however, all patient suspected of having PVFMD should undergo flexible laryngoscopy. Visualization of narrowing (adduction) of the vocal cords with both inspiration and expiration, especially exhalation is diagnostic. Behavioral therapy with LCT is vital for treatment as well as treating underlying causes that may be contributing to PVFMD. Figure 1 shows a suggested algorithm in assessing dyspnea in the athlete.

Compliance with Ethics Guidelines

Conflict of Interest David Krey and Thomas Best declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent No human or animal studies performed by the authors:

This article does not contain any studies with human or animal subjects performed by any of the authors.

Human studies done by authors (but no animal studies) This article does not contain any studies with animal subjects performed by any of the authors. With regard to the authors' research cited in this paper, all procedures were followed in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000 and 2008.

Animal studies done by authors (but no human studies) This article does not contain any studies with human subjects performed by any of the authors.

With regard to the authors' research cited in this paper, all institutional and national guidelines for the care and use of laboratory animals were followed.

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- •• Of major importance

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