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SPECIAL ARTICLE

Life-threatening respiratory diseases or allergies in sport

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Abstract There is a real possibility that physical activity endangers life, due to sports practice or a mismanaged disease, but is not always taken into account. Deaths while practicing sports and risk of a fatal outcome are low, and have been associated with cardiovascular problems. However, diseases of other biological systems, as well as an individual predisposition, can lead to a high risk situation while exercising. A brief review of respiratory diseases and allergies is presented, with advice and a warning in order that the patient may practice with the highestlevel of safety. It is also proposed the introduction of the life-threatening disease concept inthe field of sports medicine is also proposed, with a rationalization of the concept of deathin sport.

PALABRAS CLAVE
Enfermedad de riesgo vital;
Muerte súbita;
Asma;
Anafilaxis;
Neumotórax espontáneo;

Enfermedad de riesgo vital de origen respiratorio o alérgico en el deporte

Resumen La posibilidad de que la actividad física pueda poner en peligro la vida del deportista existe, pero no siempre se tiene en cuenta. La muerte en la práctica deportiva o el riesgo de un suceso cercano a la misma son bajos, y ambos se asocian habitualmente a procesos de origen cardiovascular. En el presente artículo se realiza una revisión de las enfermedades respiratorias y alérgicas más frecuentes —asma, anafilaxia, embolismo pulmonar, neumotórax espontáneo—, dignas de una atención y una formación seria y dirigida para permitir una práctica con el máximo de seguridad. Se propone acoger el

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Tromboembolismo pulmonar

concepto de enfermedad de riesgo vital en el deporte para concienciar a los especialistas en identificar esas enfermedades, que de acuerdo con este concepto ayuden a establecer unas indicaciones y guías útiles para los portadores de esas enfermedades ante unas condiciones deportivas determinadas para asegurar un deporte sano y saludable.

Introduction

The practice of sport, either for leisure or at high-competition level, implies a good physical condition and health status. In fact, exercise can be used as a means to reduce the likelihood of disease. Not surprisingly, the systematic training and the comprehensive care of athletes, keeps them healthy, and all measures are applied to help prevent injury, ensure recovery, avoid complications of exercise-induced diseases or improve their prognosis. But, obviously, athletes are not devoid of silent congenital or hereditary disorders which may be difficult to identify in the absence of a family history. Also, some diseases that may coexist with a high-level of athletic performance can be aggravated by physical exercise.

The positive effect of exercise and a physically active lifestyle has been well documented in chronic diseases in general[1,2] and in respiratory diseases in particular[3], including asthma[4,5]. The unfortunate occurrence of death of an apparently healthy athlete, while exercising, seems to question the basis of a healthy lifestyle, posing a real paradox. These traumatic incidents mobilize specialists in the preventive diagnosis of conditions that can cause sudden death in sport. The words of Tunstall Pedoe are quite pertinent in this respect: "Is exercising a normal human activity, or is it something only to be sampled under doctors' orders, a dangerous medicine?"[6].

The concept of death in sport

In a recent survey by the National College Athletic Association (NCAA), more than 50% were accidental, 16% were of cardiac origin, 14% were related to other medical problems, and the rest were due to psychosocial or unknown causes. As practitioners responsible for the health of athletes, we must pay attention to all factors that may be controlled with the aim of preventing death of the athlete during sport activities. In this sense, death may occur during sports due to accidents, due to the aggravation pre-existing disease as a direct result of the exercise, due to the specific sport practice taking place in conditions that stress a system, whether there is an underlying pathology or not, and leading to the inability of the individual to adapt, or due to a voluntary reason (homicide or suicide)[7].

The term sudden death (SD) has been used differently by epidemiologists, clinicians, pathologists and specialists in forensic medicine[8]. From a clinical standpoint, sudden death is regarded as a fatal outcome from natural causes within the first hour after onset of symptoms. This exclude accidents, poisonings, suicides, etc.[9]. Most of the existing literature is related to competitive athletes but SD during sport is more frequent in the general population practising leisure sports[10,11]. In fact, it appears that only a small fraction of sudden deaths in the youngest occur during competitive athletics[12]. The system responsible for the failure may vary; however, sudden cardiac death accounts for over 90% of all cases of sudden death[13]. For that reason, often the term SD transcends to sudden cardiac death. Hence, both among the lay and even in scientific forums, sudden death is considered only to be cardiogenic. Ischemic heart disease is present in over 80% of individuals who die suddenly, especially after 35-40 years. The actual incidence of sudden death varies from country to country according to the prevalence of ischemic heart disease, being much more frequent in Northern European countries and the United States than in the Mediterranean area. According to the WHO, the incidence of sudden death from heart disease in industrialized areas varies from 20 to 160 per 100.000 inhabitants per year among men aged 35 to 64 years[14].

The sudden death of an athlete during sports activities, athlete sudden death (ASD), is a special concept that extends the interval of occurrence of SD, considering ASD as that which happens in the first 24 hours after a sporting event[6,15]. The purpose of this increase in the time-line, would be to include in this evaluation, all conditions that may lead to the fatal outcome. Consequently, establishing the relationship between exercise and the underlying condition leading to death will allow us to institute preventive, diagnostic and therapeutic models to improve the outcomes for the athlete (Table 1).

The prevalence of ASD in competitive athletes has been estimated at 0.4-2/100,000 participants per year[16-18], while in the recreational athlete, the incidence is calculated as 0.16-4.46/100,000 individuals[11,19-21]. As in the non-athlete, in the younger age-group most deaths are of cardiovascular origin, this is associated with unsuspected structural heart disease[22]. It should be mentioned that if the definition of SD is complicated, this is even more so for ASD. In most cases, research on ASD is based in data appearing in the press, in-

Table 1 An approach to the definition of different events with a common end

Sudden death (SD)	Fatal outcome from natural causes within the first hour after onset of symptoms
Sudden death in sport (SDS)	Sudden death during the sports activity[a]
Athlete's sudden death (ASD)	Sudden death of the athlete with a scheduled workout, theoretically well-structured and targeted, which in most cases, but not always, is of cardiac origin. It may have an underlying pathology that causes sudden death, but also an idiosyncratic aetiology, for some individuals who are more susceptible, when the practice of certain sports or work intensities occurs simultaneously with key trigger factors
Sport life threatening disease (SLTD)	A condition in which the practice of sport by the exercise itself or because it is performed under extreme conditions or exposure, acts as the main trigger, essential co-factor or cause of a worsening of the disease that can even lead the subject to a fatal outcome

[a] In some instances, this was considered to be death during the 24 hours after the onset of symptoms, but there is no current consensus about this.

ternet and emergency records[23]. This suggests that there is a possible underestimation of the number of cases.

The ASD has mainly been related to cardiac conditions, and this aspect is especially evaluated in athletes[24,25], using complementary tests as ECG, exercise ECG and/or echocardiography[26]. Most physicians involved in screening athletes recognize the limitations of pre-participation screening in detecting those at risk for sports-related morbidity and mortality. A thorough clinical history is essential to enable the identification of athletes who might be at risk[27]. But death in the practice of physical activity may be triggered by non-cardiogenic causes. Exercise strains other systems beyond the cardiovascular system to adapt to physical effort, such as the metabolic, nervous, endocrine, and respiratory systems. A thermal shock[28], cerebral haemorrhage[29], a life-threatening haemoptysis[30], an anaphylactic shock associated with exercise[31] or those related to extreme environments in addition to a chronic illness or not[32,33], may all act as potential triggers.

At present, the concept of unknown disease, undiagnosed condition or prior excellent health status in relation to SD, become obsolete in the light of technological advances in preventive diagnosis. Clearly, it is important that the identification process is undertaken, meaning that the diagnosis is made, that it is plausible to achieve or that it is actively pursued[33-35]. Therefore, from a preventive point of view it would be more useful work with the concept of 'life-threatening diseases' (LTD) instead of SD. This means that under certain conditions such diseases may lead to a fatal outcome. In the field of Medicine of Physical Activity and Sport, exercise is the main trigger, co-factor or fundamental cause, allowing by this definition to work on the prevention of sudden death which may not be unexpected.

Risk of respiratory death during exercise

Whenever a specialist is consulted by a patient with respiratory disease who practices or intends to practice sport, straining leisure activities or any physical exercise which entails stress of adaptation systems, he/she is responsible for assessing the patient's characteristics, the disease, medication and the possible influence of the exercise and the environment where it will be performed[36]. A history of spontaneous pneumothorax[37,38], certain pulmonary birth defects[39,40], lower respiratory tract infection[41,42], chronic airflow limitation with/without desaturation[43], prior sensitization to certain foods, insect stings and particularly asthma[44], or parenchymal tissue weakness due to disease or to treatments, are common conditions which should be carefully evaluated. In the area of pulmonology, most diseases cause shortness of breath during exercise but will never jeopardize the patient's life as the respiratory disease itself limits the intensity of exercise. But it is also true, that in some diseases, this must be considered, especially if in addition to the physical stress, there is an adverse environment to which the subject is exposed[45,46]. Current trends in leisure activities and travel, such as trekking, hiking, mountaineering[47], scuba diving[48,49], or balloon trips[50], will expose patients to the limits of their cardiorespiratory system. It is not necessary to excessively highlight special cases that do not really justify an overzealous attitude to pre-participation screening, but these cases should alert the athlete of the desirability of following the advice of the medical practitioner.

The three most important life threatening conditions in respiratory and allergy medicine are *asthma*, *pulmonary embolism* and *exercise-induced anaphylaxis*. We should also take into consideration some nuances regarding spontaneous pneumothorax.

Asthma

Asthma affects 300 million people worldwide and it is estimated that 250,000 die annually, mostly due to under-diag-

nosis, inappropriate treatment or delay in medical care during the fatal crisis[51]. In Spain, asthma prevalence is around 0.4/100,000 inhabitants for males and 0.1 for females between the ages 5 to 34 years[52]. These rates are similar in other countries of equal socioeconomic status, although there has been a general drop in life-threatening asthma[53]. Hospital admissions for acute, exercise-induced life-threatening asthma is around 0.2% of all causes in Spain (300 to 350 cases), and 0.5% in Latin America (600 to 700 cases)[54]. The age range is wide and it includes, not only exercise induced asthma, but any kind of physical exertion. Nevertheless, there are no specific registers of asthma-related deaths during sport. This lack of information may seem due to a lack of interest, but the reality is that it is extremely difficult to retrieve data in relation to such fatalities[55].

Exercise is an intrinsic aspect of any sport activity, and also one of the trigger factors of an asthma attack. Under controlled circumstances, i.e., controlled asthma, this crisis is self-limited and relatively easy to prevent with prophylactic measures and appropriate drug therapy[56]. But severe exacerbation of asthma by upper airway infections (65% of cases), by exposure to aeroallergens (3.6%) or to drugs (0.5%), are triggers that increase the sensitivity of the respiratory and digestive system to the effort[54], especially in athletes[57], and drive the crisis to an unusual level of severity. In such cases, in which several factors are involved, it may be difficult to identify the most relevant one, and exercise may be overlooked.

Pulmonary embolism

A cardiovascular disease that targets the lung is pulmonary embolism (PE). Onset during sport is not unusual and can be manifested in various ways. Diver's decompression syndrome[58], post-traumatic fat pulmonary embolism[59] or postoperative pulmonary embolisms are examples of well-established LTD, which need immediate therapeutic intervention. Pulmonary embolism is not often recognised as the third most common cardiovascular disease after myocardial infarction and stroke, but this needs to be acknowledged. Death rates from PE exceed those from myocardial infarction, as myocardial infarction is much easier to detect and to treat[60]. The diagnosis of PE in the athlete is more complicated, when its onset is subacute or manifests itself as a chronic pulmonary embolism. PE can often mimic other respiratory diseases, and can even be aligned with asthma, delaying the diagnosis. PE should always be suspected in subjects with a genetic thrombophilic background, experiencing sudden dyspnoea, usually without other signs. This is of specific concern in subjects with coagulation disorders, or those with a predisposition to deep venous thrombosis, with compromised venous return, after long trips, dehydration, recent surgery, under anovulatory treatment or anabolic steroids[61]. Systemic inflammation due to other processes results in activation of coagulation, due to tissue factor-mediated thrombin generation, downregulation of physiological anticoagulant mechanisms, and inhibition of fibrinolysis[62] can also act as a trigger for PE. This is also the case when thromboembolism is an extra-intestinal manifestation of an inflammatory bowel disease[63]. All these factors have to be taken into account and appropriate diagnostic and preventive measures put into place. Depending on the risk profile of individuals, the use of graduated compression stockings and/or pharmacological interventions may be recommended[64].

Exercise induced anaphylaxis

One of the allergic disorders which may cause acute cardiorespiratory events and can cause sudden death in athletes is exercise induced anaphylaxis[31,65]. Anaphylaxis is defined as a serious allergic reaction that is rapid in onset and might cause death[66]. In most cases, there is an underlying food allergy, asymptomatic or mild when food is consumed at rest, but that causes symptoms during physical exertion. It is estimated that the percentage of exercise-induced anaphylaxis is around 2.5-5% of all anaphylaxis cases attended in emergency departments[67,68]. The most well characterised syndrome is wheat-dependent exercise-induced anaphylaxis[69], although in the Mediterranean countries, fruit, nut or vegetable allergy due to sensitisation to lipid transfer proteins is also prevalent[70,71]. Therefore, this condition should be considered in patients presenting with urticaria, along with respiratory, digestive or cardiovascular symptoms occurring during physical exertion[72].

At present, sudden death from **pulmonary embolism**, asthma or anaphylaxis, is not, in principle, considered a cause of sudden death, although it may develop suddenly and unexpectedly. What seems clear is that at present, deaths from asthma attacks during exercise may not be adequately assessed, and co-factors such as food allergy, infections, inhalant allergen exposure, concomitant medications or even hymenoptera sting allergy may be overlooked. In any case, the underlying disease may be well known to the patient and its physician, making it possible to establish adequate preventive measures.

A first step in the case of asthmatic patients is to evaluate the risk of acute exacerbation. Prior hospitalisation, under-treatment, and obesity are known risk factors for exacerbation[73]. Asthma death has been associated with the number and severity of previous exacerbations, prescription of three or more medications or oral corticosteroids, and psychosocial problems[74]. Consequently, all these factors should be appraised when evaluating the possibility of practising exercise by these patients.

In short, the common denominator of asthma deaths in sport is based on the presence of severity of the underlying disease, moderate or severe persistent asthma, low adherence to treatment and an underestimation of the disease severity[75]. Some subgroups of patients, such as those underestimating the severity of their asthma, due to psychosocial conditions, and those in at-risk age groups, such as pre-adolescence and adolescence, may be tackled through education and adequate long-term monitoring.

Spontaneous pneumothorax

Finally, some consideration needs to be given for exercise prescription in patients who have suffered a **spontaneous pneumothorax**. Pneumothorax is the presence of air in the pleural space and primary spontaneous pneumothorax is defined as the spontaneously occurring presence of air in the pleural space in patients without any clinically apparent underlying lung disease. Even if physical activity is prescribed and undertaken, spontaneous pneumothorax usually occurs at rest[76]. The risk of death is extremely low. Hospital admission rates for pneumothorax from 1991 to 1995 were 16.7/100,000 per annum, whereas deaths from pneumothorax (including all high risk cases) were less than 1% of this figure at 1.3/1,000,000 per annum[77]. The risk of recurrence after a first primary spontaneous pneumothorax is estimated between 30% and 50%, male gender and smoking markedly increasing the risk[78]. The average time span between the first and second episodes is approximately 18 months (range, 4 to 35 months). Approximately one third of those who have a second pneumothorax go on to have a third episode[79]. The above information provides a theoretical basis for advising individuals who have had a previous spontaneous pneumothorax, to avoid performing sport activities in environments where the recurrence of the process could by itself, or by the isolated nature of the environment endanger the subject's life and that of his companions (i.e., diving, aerial acrobatics, balloon trips and mountain climbing)[80]. The fact that a pneumothorax has not occurred for 2 to 3 years does not ensure that it will not re-occur.

Comorbidity and climate

Through identification, education and evaluation of the patient we must assess those causes that can lead to a crisis in a patient with asthma during sports[81]. Co-morbidities such as rhinitis have to be adequately evaluated. Also, environmental conditions such as storms, rainfall, wind speed and direction, atmospheric pressure or temperature can dramatically influence the worsening of asthma while practising outdoor sports[82]. Not surprisingly, emergency room visits for asthma increase when humidity is high and atmospheric pressure is low and for pneumothorax with thunderstorms, possibly due to the rapid and important changes in air pressure, humidity, pollen concentration, air pollution, and electrostatic power as well as physical stress because of warmth, wind, or humidity[83,84]. During storms, osmotic rupture of pollen grains is increased, producing high amounts of breathable particles which may trigger allergy symptoms[84]. Similarly, cold, dry air is a well-known factor associated with asthma attacks. All these factors are summarised in Table 2.

Conclusion

The occurrence of sudden cardiac death is rare in childhood and adolescence; however, it must be taken into account in children and adolescents with asthma, since half of cases occur in the age range 10 to 20 years, with no difference between practice, competition sports or leisure. This factor is of importance, as not all children practice competition sports, however, all kids exercise while they play.

Table 2 Circumstances related to episodes of exacerbation of asthma and fatal asthma attack

	Exacerbation of asthma	Fatal asthma
All out causes		
Sport activities	Intrinsic asthma severity	Hospitalization in the last year
	Level of adherence to treatment	Patient's psychosocial problems
	Non sport activities	Asthma and rhinitis comorbidity
Three or more prescription drugs		
	Neutrophilic asthma	Start of oral corticosteroids
	Low sociocultural level	
	Climate-related aspects	
	Menstrual period[85]	
	Obesity and low physical condition	

The relationship between respiratory and allergic diseases with exercise is complex. The message for patients should be clear, and although active participation in sport should not be discouraged, it should reinforce the concept that life-threatening disease can be controlled with appropriate measures.

Whether deaths that occurred during exercise caused by respiratory and allergic causes are considered sudden death or not should be a matter of concern and debate. This consideration would allow a better identification and evaluation of susceptible individuals and thereby create an evaluation model that is as systematic and thorough as seen for cardiovascular conditions.

Conflict of interests

The authors have no conflicts of interests to declare.

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