RESPIRATORY IMPACT OF A GRAND TOUR: INSIGHT FROM PROFESSIONAL CYCLING

Hayden Allen MRes[1], Oliver J. Price PhD[1], Jon Greenwell MD[1,2], James H. Hull PhD FACSM[3,4]

[1]Clinical Exercise and Respiratory Physiology Research Group, Carnegie School of Sport, Leeds Beckett University, Leeds, United Kingdom (UK); [2]English Institute of Sport, London UK; [3]Department of Respiratory Medicine, Royal Brompton Hospital, London, UK; [4]Institute of Sport, Exercise and Health (ISEH), UCL, London, UK

Corresponding author:

Dr Oliver J. Price BSc (Hons.) MRes PhD FHEA

Clinical Exercise and Respiratory Physiology Research Group

Carnegie School of Sport, Leeds Beckett University

Leeds, LS6 3QT

Tel: +44 (0) 113 8123 532

E-mail: o.price@leedsbeckett.ac.uk

Twitter: @oliverjprice

Manuscript word count: 3335; **Abstract word count:** 264.

Running title: Respiratory function in professional cyclists.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the commitment and support of the World Tour professional cyclists and team staff involved in the completion of this study.

ABSTRACT

Purpose: The aim of this study was to evaluate respiratory function and symptom perception in professional cyclists completing a Grand Tour (GT). **Methods:** Nine male cyclists completed La Vuelta or Tour de France (2018/19). At study entry, airway inflammation was measured via fractional exhaled nitric oxide (FeNO). Respiratory symptoms and pulmonary function were assessed prior to the first stage (Pre-GT), at the second rest day (Mid-GT) and prior to the final stage of the GT (Late-GT). Sniff nasal inspiratory pressure (SNIP) was assessed at pre and late-GT timepoints. **Results:** Seven cyclists reported respiratory symptoms during the race (with a prominence of upper airway issues). Symptom severity increased either mid or late-GT for most cyclists. A decline in FEV_1 from pre-to-mid GT (-0.27 ± 0.24 l, -5.7%) (P = 0.02) and pre-to-late GT (-0.27 ± 0.13 l, -5.7%) (P < 0.001) was observed. Similarly, a decline in FVC (-0.22 ± 0.17 l, -3.7%) (P = 0.01) and FEF_{25-75} (-0.49 ± 0.34 l/s, -11%) (P = 0.02) was observed pre-to-late GT. Overall, eight (89%) and six (67%) demonstrated a clinically meaningful decline (> 200 ml) in FEV_1 and FVC during the GT follow-up, respectively. SNIP remained unchanged pre-to-late GT (n = 5) however a positive correlation was observed between ΔSNIP and ΔFVC (r = 0.99, P = 0.002). **Conclusion:** GT competition is associated with a high prevalence of upper respiratory symptoms and a meaningful decline in lung function in professional cyclists. Further research is now required to understand the underpinning physiological mechanisms and determine the impact on overall respiratory health and elite cycling performance and recovery.

Key words: Cycling, Respiratory, Physiology, Elite, Performance

DECLARATIONS

Funding

Nil relevant.

Competing interests

The authors have no real or perceived conflict of interest in respect of this manuscript.

Availability of data

All data relevant to the study are presented in this article. The data are not available due to the potential for a breach of confidentiality.

Code Availability

Not applicable

Contribution statement

OP, JG, JH were involved in the conception and design of the study. HA and JG acquired the data. All authors were involved with drafting and critical revision of manuscript and final approval of the version to be published. The results of the study are presented clearly, honestly, and without fabrication or falsification.

ABBREVIATIONS

EIB	Exercise-induced bronchoconstriction
FEF_{25-75}	Mean forced expiratory flow between 25% and 75% of forced vital capacity
FeNO	Fractional exhaled nitric oxide
FEV_1	Forced expiratory volume in one second
FVC	Forced vital capacity
GT	Grand tour
ICS	Inhaled corticosteroid
IQR	Interquartile range
LTRA	Leukotriene receptor antagonist
PEF	Peak expiratory flow
PPB	Parts per billion
RMF	Respiratory muscle fatigue
SABA	Short-acting beta-2 agonist
SNIP	Sniff nasal inspiratory pressure
TDF	Tour de France
UCI	Union Cycliste International
VAS	Visual Analogue Scale
VO_{2max}	Maximal Oxygen Uptake
Vuelta	Vuelta a España

INTRODUCTION

Grand Tours (GTs) are major three-week annual cycling stage races (total distance > 3,000 km) that are recognised to be amongst the most challenging endurance sporting events in the world (Lucía et al. 2003). Indeed, professional GT cyclists are often considered to represent the 'elite of the elite' and typically demonstrate advanced cardio-respiratory physiology (i.e. maximal oxygen uptake (VO_{2max}) > 70 $ml.kg^{-1}.min^{-1}$) (Bell et al. 2017; Sanders and Heijboer 2019).

The physiological load endured during a GT is influenced by the type of stage (i.e. flat, semi-mountainous, mountain, and time trial) and a rider's specialist background. In addition to locomotor muscle fatigue, it is now recognised that participation in a GT places significant metabolic demands on the respiratory system (Fernández-García et al. 2000; Dominelli et al. 2019). Moreover, GT riding is punctuated by periods of maximal intensity exercise, required in certain critical race scenarios (i.e. establishing a breakaway or sprint finish) (Abbiss et al. 2013) that can elicit ventilation rates > 150 l/min (Lucia et al. 2002). It is therefore not uncommon for highly trained endurance athletes to develop evidence of expiratory airflow limitation (Derchak et al. 2000; Foster et al. 2014) which is associated with a considerable and sustained increase in work of breathing and potential for respiratory muscle fatigue (RMF) (Guenette et al. 2007).

In addition to the physiological stress of sustained exercise hyperpnoea from this type of endurance sport, GT cyclists are also regularly exposed to variable environmental conditions (i.e. fluctuations in temperature and humidity), aeroallergens and combustion engine particulate matter arising from the close proximity of team support cars +/- media motorbikes. This exposure is pertinent from a respiratory health perspective as it has previously been argued that this type of endurance exercise may actually result in airway changes that are akin to an 'injury'; i.e. promoting the development of airway hyper-responsiveness and allied respiratory symptoms (Price et al. 2013). In this respect, it has been recognised for some time that asthma or exercise-induced bronchoconstriction (EIB) (a condition

characterised by transient lower airway narrowing) occurs in up to one in five elite-endurance athletes and is prominent in competitive cyclists and triathletes (Dickinson et al. 2005; Dickinson et al. 2006b).

It is therefore perhaps not unsurprising that professional cyclists often report a heightened perception of breathlessness, troublesome end-race cough and/or the sensation of having 'smaller lungs' during and/or following GT competition (variety of personal communications). This anecdotal evidence corroborates with recent observations of a deterioration in lung function and the presentation of troublesome respiratory symptoms following single and multi-stage ultra-endurance sporting events (Vernillo et al. 2015; Tiller et al. 2019; Stensrud et al. 2020). Although symptom-perception is recognised to correlate poorly with objective physiological testing (Rundell et al. 2001; Simpson et al. 2015; Price et al. 2016a; Price et al. 2016b), the potential for GT competition to impair respiratory function remains a concern. Indeed, repeated acute exacerbations in athletes are associated with a deterioration in airway health (Vergès et al. 2004) whereas respiratory symptoms may affect performance by decreasing sleep quality and race recovery (Kennedy et al. 2016). Furthermore, bronchoconstriction +/- RMF has the potential to limit exercise tolerance through perceptual and physiological mechanisms (Romer and Polkey 2008; Price et al. 2014b).

Despite these concerns, to date there has been little published data detailing the respiratory impact of GT participation. We therefore undertook this study with the aim of providing contemporary insight concerning the impact of a GT on respiratory function in professional male cyclists. It was hypothesised that over the course of the event, cyclists would experience a decline in respiratory function and perceive an increased frequency and severity of symptoms.

METHODS

Study population and experimental design

Eleven Union Cycliste Internationale (UCI) World-Tour registered professional male cyclists were invited to participate in this pragmatic, real-world, observational trial, during the Vuelta a España (Vuelta) or Tour de France (TdF) between 2018-19. All cyclists were free from respiratory tract infection two weeks prior to study entry with no history of cardiac, metabolic or psychiatric disease or any other significant medical condition except allergy, mild asthma or EIB; five cyclists had a prior EIB diagnosis of which one also suffered from seasonal allergic rhinitis. Of those with EIB, all were prescribed inhaled corticosteroid (ICS) maintenance therapy, and four were prescribed a short-acting bronchodilator (short-acting beta-2 agonists (SABA) or anti-cholinergic) to be used on an 'as-needed' basis. Three were prescribed oral antihistamines, and one was prescribed a leukotriene receptor antagonist (LTRA). All cyclists maintained any regular medication use, as prescribed, throughout the study.

At study entry, baseline airway inflammation was measured via fractional exhaled nitric oxide (FeNO). Respiratory symptoms and pulmonary function were assessed at rest on three separate occasions: (i) p.m. 48-hours prior to the GT (Pre-GT), (ii) p.m. on the second rest day (i.e. 17 days following the start of the race) (Mid-GT) and (iii) a.m., prior to the final stage of the GT (Late-GT). Respiratory muscle strength was assessed pre-GT and late-GT. The study was approved by Leeds Beckett University ethics committee (ethics ID: 50593) and all cyclists provided written informed consent.

Clinical assessment

Respiratory symptoms were evaluated using visual analogue scales (VAS) (Gift 1989; Lee et al. 2013). The VAS assessed perceptions of cough, throat discomfort, voice changes, breathlessness and difficulty swallowing, eating or drinking using a 100-mm scale. Perceived changes to taste and smell were determined via either a yes or no response.

Lung function and airway inflammation

Lung function was assessed at rest (> 2 hours following any prior exercise, > 4 hours from SABA administration) using seated, maximal forced flow-volume spirometry (MicroLoop Mk8 spirometer; Micro Medical, Carefusion, 2010) with reference values employed in accordance with international guidelines (Quanjer et al. 2012; Graham et al. 2019). A change in FEV_1 and FVC > 200 ml was considered a minimal clinically important difference (Bonini et al. 2020). Airway inflammation was assessed via the measurement of FeNO (NObreath; Bedfont Scientific, Kent, UK) and evaluated against established thresholds: normal: < 25 ppb; intermediate: 25 – 50 ppb; high: > 50 ppb (Dweik et al. 2011).

Sniff-nasal inspiratory pressure

Inspiratory muscle strength was determined via sniff nasal inspiratory pressure (SNIP) manoeuvres (MicroRPM, Micro Medical Ltd, Kent, UK) in accordance with international guidelines (Laveneziana et al. 2019). In brief, cyclists exhaled to functional residual capacity prior to performing a maximal sniff manoeuvre through the contralateral, non-occluded, nostril. In order to obtain reproducible efforts (± 10%) and minimise the potential for RMF, a minimum of two, and a maximum of eight manoeuvres was performed with the maximum value recorded for analysis.

Statistical analysis

Data are presented as mean ± SD and median (interquartile range (IQR)) for continuous outcomes dependent on normality. Baseline between group differences (i.e. healthy vs. EIB) were evaluated using an independent t-test. Pre-GT, mid-GT and late-GT spirometric indices were assessed using a one-way repeated measures ANOVA. Pre-to-late GT changes in SNIP were evaluated using a paired t-test. The perception of respiratory symptoms was quantified as a non-zero VAS response and analysed over time using a Cochran's Q test. The association between symptom severity (individual symptoms and total VAS score) and lung function were evaluated using Pearson's and Spearman's rank correlations. Data were analysed using SPSS Statistics 26 statistical software package (SPSS Inc., Version 26, Chicago,

IL) and GraphPad Prism Version 8.0 (GraphPad Software, San Diego, California, USA). Data are presented as mean ± SD and $P < 0.05$ was considered statistically significant.

RESULTS

Study population and race information

Two cyclists withdrew from the study due to injury and thus nine cyclists completed the GT and study measurements. Specifically, four cyclists completed the Vuelta and five completed the TdF. Race distance and duration was comparable between events: Vuelta 3,255 km and 84 hours; TdF 3,480 km; and 85 hours; Vuelta + TdF combined average: 3,380 ± 119 km and 85 hours. Clinical characteristics are presented in Table 1.

Respiratory symptoms

A total of seven cyclists (78%) were symptomatic on at least one occasion, with four cyclists reporting respiratory symptoms at each time-point. Cough, voice changes and breathlessness were reported by five cyclists and throat discomfort by four cyclists at one or more time-points. One cyclist reported difficulty swallowing at all time-points. Of note, voice changes were reported concurrently with cough on six out of seven occasions, whereas throat discomfort and breathlessness coincided with the perception cough on five occasions. Although symptom frequency was unchanged over the course of the event (Table 2), symptom severity increased either mid or late-GT for most cyclists (Figures 1a-e).

Lung function, airway inflammation and respiratory muscle strength

All cyclists had normal lung function pre-GT, with no evidence of expiratory airflow limitation (FEV_1 > lower limit of normal (LLN)) (Table 1). Five cyclists had an elevated FeNO pre-GT. Four cyclists (n = 2 with EIB) were classified as intermediate and one cyclist with EIB was classified as high. No difference was observed in spirometric indices between those with or without EIB. A decline in FEV_1, FVC and FEF_{25-75} was observed over time ($P < 0.05$) (Figures 2a, b, e). However, no change in PEF and FEV_1/FVC were observed over time ($P > 0.05$) (Figures 2c, d). Specifically, a decline in FEV_1 from pre-to-mid GT (-0.27 ± 0.24 l, -5.7%) ($P = 0.02$) and pre-to-late GT (-0.27 ± 0.13 l, -5.7%) ($P < 0.001$) was observed. Similarly, a decline in FVC (-0.22 ± 0.17 l, -3.7%) ($P = 0.01$) and FEF_{25-75} (-0.49 ± 0.34 l/s, -11%) ($P = 0.02$) was observed pre-to-late GT. Importantly, eight and six cyclists demonstrated a

decline in FEV_1 > 200 ml at mid-GT (n = 5 with EIB) and late-GT (n = 4 with EIB), respectively. Likewise, six and five cyclists demonstrated a decline in FVC > 200 ml at mid-GT (n = 4 with EIB) and late-GT (n = 3 with EIB), respectively. Five cyclists completed SNIP measurements. Respiratory muscle strength remained unchanged from pre-to-late GT (90 ± 22 vs 81 ± 18 cm H_2O, $P = 0.39$) (Figure 3). Although a positive correlation was observed between ΔSNIP and ΔFVC ($r = 0.99$, $P = 0.002$), no relationship was observed with any other spirometric parameter.

Respiratory function vs. symptom perception

The severity of pre-GT symptoms did not correlate with baseline airway inflammation ($P = 0.10$) or lung function parameters ($P > 0.05$). Likewise, pre-to-mid GT and mid-to-late GT changes in lung function were not associated with changes in cough, throat discomfort, voice change and breathlessness when evaluated in isolation ($P > 0.05$). However, changes in PEF were associated with changes in total VAS score pre-to-mid GT ($r = -0.85$, $P = 0.03$) and mid-to-late GT ($r = -0.97$, $P = 0.006$). No association between the changes in total VAS and changes in FEV_1, FVC, FEV_1/FVC or FEF_{25-75} were observed ($P > 0.05$). Pre-to-late GT changes in total VAS score were not associated with changes in SNIP.

DISCUSSION

This pragmatic and real-world study revealed that in professional cycling, participation in a GT is associated with a high prevalence of troublesome upper airway and respiratory symptoms and a concurrent reduction in some indices of respiratory function. Specifically, in a cohort of professional cyclists, we found a reduction in FEV_1 at mid and late-GT, a pre-to-late GT decline in FVC and FEF_{25-75} and a relationship between pre-to-late change in FVC and SNIP (a marker of respiratory muscle strength). The reasons underpinning these changes remain to be determined but highlight the presence of respiratory dysfunction and functional impairment, that may be relevant in the context of elite cycling performance and race recovery.

The respiratory system is typically considered over-engineered for the demands of intense exercise (Dempsey et al. 2020) and it is common for elite endurance athletes to have 'supra-normal' lung function (i.e. whereby capacity exceeds upper predicted limits) (Medelli et al. 2006; Bonini et al. 2007; Holmberg et al. 2007). Indeed, even in athletes with a confirmed diagnosis of asthma or EIB - the degree of impairment only becomes apparent following an exercise or indirect bronchial provocation challenge (Price et al. 2014a). In support of this concept, all cyclists in the present study (including those with EIB) had normal baseline lung function. However, a clinically meaningful (> 200 ml) (Bonini et al. 2020) decline in FEV_1 and FVC was observed in eight (89%) and six (67%) cyclists during GT follow-up, respectively. The pre-to-late GT reduction in FVC (~ 4%) is comparable to the recent findings of Tiller and colleagues (Tiller et al. 2019), who observed a decline in resting FVC (~ 6%) in recreational runners following the completion of nine consecutive marathons over a nine day period. The authors suggested this finding may be explained by a non-significant decline in maximal expiratory mouth-pressure, attributed to a perturbation in calcium availability within the respiratory muscles (Tiller et al. 2019). Similar findings have previously been observed following exhaustive time-trial exercise in well-trained cyclists (Romer et al. 2006). It is therefore plausible to speculate that the cumulative duration of a GT (~ 80 hours) with extended periods > 70% VO_{2max} (Fernández-García et al. 2000) may contribute to impaired respiratory muscle function. Although the relationship between pre-to-late GT

ΔFVC and ΔSNIP observed in the current study may indicate an interplay between changes in muscle strength and lung volume - the dataset was modest and a significant within-group reduction in SNIP was not found. Thus, other factors are likely to be relevant, including stresses placed on the airway tract and ventilatory system on a daily basis during a GT.

The decline in FEV_1 (~ 6%) observed in the present study is similar in magnitude to the reductions in FEV_1 observed following a sport-specific exercise challenge in endurance athletes (~ 6%) (Dickinson et al. 2006a; Knöpfli et al. 2007). Although bronchoconstriction typically subsides within a short-period of time following acute exercise (~ 30 - 60 mins) (Parsons et al. 2013), the potential for repeated acute exacerbations of EIB to induce a chronic decline in lung function cannot be ruled out. In this regard, GT cycling results in a ventilation rate far exceeding the capacity of the upper airway (~ 40 l/min) (Niinimaa et al. 1980) that exposes the lower airways to unconditioned air and noxious environmental stimuli (Rundell et al. 2015) - which can act to desiccate the airway lining and promote airway inflammation and bronchial obstruction (Price et al. 2013; Rundell et al. 2018). Moreover, Simpson and colleagues (Simpson et al. 2017) have previously reported a reduction in FVC following mild whole-body dehydration (~ 2.5%), which is consistent with the typical daily end-stage average fluid loss (~ 2.8%) reported in professional cyclists (Tammie et al. 2007). It is thought that dehydration may elicit the redistribution of fluid away from the airway surface and impair small airway function and lung emptying (Simpson et al. 2017). Pertinent to a GT, repeated acute airway stress is recognised to elicit airway injury and/or airway smooth muscle remodelling (Kippelen and Anderson 2012), which may have long-term implications for airway health (Rundell 2004; Vergès et al. 2004; Bougault et al. 2018).

It is also important to highlight that changes in lung function may also relate to an increased parasympathetic tone that is recognised to occur following acute high-intensity exercise (Seiler et al. 2007) and chronic physiological strain (Pichot et al. 2002; Le Meur et al. 2013). Indeed, it has previously been suggested that heightened parasympathetic activity may actually increase basal bronchomotor tone

which is associated with an increased susceptibility to develop bronchoconstriction (Moreira et al. 2011).

The prevalence and increased severity of respiratory symptoms supports previous findings observed in endurance athletes during the competitive season (Kennedy et al. 2016). One third of cyclists reported cough mid-GT which subsequently increased to almost half late-GT. Although not fully understood, it is thought that mechanical stimulation of receptors in the lung (Widdicombe et al. 2009) or direct irritation of receptors in the upper airway (Irwin et al. 2006) during periods of high ventilation may cause exercise-induced cough in susceptible individuals (Hull et al. 2017). A novel finding is the prominence of upper airway focused symptoms; almost all athletes reported voice changes or throat discomfort concurrent to cough at mid and/or late-GT performance. Symptom severity during, and late-GT, was elevated from baseline and in most cases higher mid-GT compared to late-GT. Whilst changes in overall symptom severity demonstrated a correlation with changes in PEF (a measure influenced by upper airway dysfunction) that may suggest an influence from lung function, no differences in PEF were observed over time. In addition, the severity of respiratory symptoms has previously been reported to increase in the presence of environmental stressors (Bogaerts et al. 2005), that may be pertinent for cyclists during mid-GT, compared to the later in the event.

Impact and practical implications

The decline in lung function and increased severity of respiratory symptoms is potentially concerning for GT performance. Indeed, lower resting lung function has previously been associated with expiratory airflow limitation in endurance athletes (Vergès et al. 2005), that alters operating lung volumes, and leads to a corresponding reduction and increase in the contractile efficiency and metabolic demand of the respiratory muscles (Aaron et al. 1992). The observed impairment to respiratory function during GT has the potential to induce a respiratory muscle metaboreflex (Sheel et al. 2001; Dominelli et al. 2017) and in turn, exacerbate locomotor muscle fatigue and impair endurance performance (Harms et al. 2000; Babcock et al. 2002). In addition, respiratory symptoms have been reported to affect sleep quality in

elite athletes (Kennedy et al. 2016), that may further impair performance (Fullagar et al. 2015). It is also important to recognise that all cyclists with EIB were prescribed pharmacological inhaler therapy, and thus it is plausible to speculate that if medication were to be withheld, the deleterious impact of GT competition on respiratory function may be even greater. Overall, our findings indicate that the monitoring of respiratory function during professional cycling stage racing is warranted in order to implement strategies to preserve lung function and maintain respiratory health. Although it has previously been reported that deteriorations in lung function may reverse following retirement from elite sport (Helenius et al. 2002), optimising respiratory health during an athlete's career remains a priority (Price and Hull 2014). It is also logical but speculative to acknowledge that persistent symptoms may ~~impact~~ affect recovery and cause distraction and cognitive distress, thereby indirectly impacting elite performance.

Methodological considerations and future research

This study was conducted as a real-world observational study in professional cyclists, at two of the most prestigious races within elite cycling. It is acknowledged that consistency in alignment to pre-test guidance was likely variable between cyclists due to competing logistical demands (i.e. team commitments and kit preparation etc.) and although there was a small difference in the timing of measurements, the influence of diurnal variability on lung function measures cannot be entirely discounted. However, all measurements were conducted in accordance with relevant technical international guidelines and standards. Further research is warranted to substantiate these findings in association with different multi-stage endurance competitions to fully understand the time-course and mechanisms of physiological and/or pathophysiological decline in respiratory function, the proliferation of inflammatory cells and markers of airway epithelial injury (i.e. club cell secretory protein-16). Moreover, ideally a more comprehensive battery of tests would be utilised (e.g. lung volumes +/- oscillometry) and neural drive electromyography measures conducted, allied with detailed measures of small airway function (e.g. multiple-breathe nitrogen washout or partitioned FeNO) - these tests are not easy to deliver nor achievable within the setting of a moving race scenario. However, measurements of

inspiratory and expiratory muscle strength (via mouth-pressure metres) and maximal voluntary ventilation manoeuvres would certainly be feasible and should therefore be considered in the design of future studies.

Conclusion

In summary, our findings indicate that participation in GT competition is associated with a high prevalence of upper respiratory symptoms and a meaningful decline in lung function in professional cyclists. Further research is now required to understand the underpinning physiological mechanisms and determine the impact on overall respiratory health and elite cycling performance and recovery.

TABLE HEADERS

Table 1. Clinical characteristics and baseline lung function.

Table 2. Frequency of perceived respiratory symptoms.

Table 1.

Variable	Mean (SD)		
Age (yrs.)	30	±	3
Height (cm)	179.2	±	4.8
Body mass (kg)	68.9	±	6.3
BMI ($kg.m^{-2}$)	21.4	±	1.0
FEV_1 (L)	4.81	±	0.54
FEV_1 (% predicted)	105	±	7
FVC (L)	5.97	±	0.77
FVC (% predicted)	107	±	11
PEF (L/s)	10.32	±	1.35
PEF (% predicted)*	99		13
FEV_1/FVC (%)	81	±	6
FEV_1/FVC (% predicted)	98	±	7
FEF_{25-75} (L/s)	4.71	±	1.05
FEF_{25-75} (% predicted)	102	±	19
FeNO (ppb)*	28		19

Data presented as mean ± SD. * denotes median IQR.

Table 2.

VAS measure	Frequency of non-zero response		
	Pre-GT	Mid-GT	Late-GT
Cough	0	3	4
Throat Discomfort	1	3	3
Voice Changes	2	3	3
Breathlessness	3	3	2
Difficulty swallowing, eating or drinking	1	1	1
Changes in smell	0	1	1
Changes in taste	0	0	1

FIGURE CAPTIONS

Figure 1. VAS score of non-zero responders for cough (a), throat discomfort (b), voice changes (c), breathlessness (d) and difficulty swallowing (e).

Figure 2. GT changes in FEV_1 (a), FVC (b), PEF (c), FEV_1/FVC (d), FEF_{25-75} (e) (■ - mean ± SD; ▲ - median ± IQR). *denotes significant difference from pre-GT, $P<0.05$.

Figure 3. Individual (●) and group (■) pre-to-late GT changes in SNIP.

REFERENCES

Aaron E, Seow K, Johnson BD, Dempsey J (1992) Oxygen cost of exercise hyperpnea: implications for performance. J Appl Physiol. 72:1818-1825 https://doi.org/10.1152/jappl.1992.72.5.1818

Abbiss CR, Menaspà P, Villerius V, Martin DT (2013) Distribution of power output when establishing a breakaway in cycling. Int J Sports Physiol Perform. 8:452-455 https://doi.org/10.1123/ijspp.8.4.452

Allen H, Backhouse SH, Hull JH, Price OJ (2019) Anti-doping Policy, Therapeutic Use Exemption and Medication Use in Athletes with Asthma: A Narrative Review and Critical Appraisal of Current Regulations. Sports Med. 49:659-668 10.1007/s40279-019-01075-z

Babcock MA, Pegelow DF, Harms CA, Dempsey JA (2002) Effects of respiratory muscle unloading on exercise-induced diaphragm fatigue. J Appl Physiol. 93:201-206 https://doi.org/10.1152/japplphysiol.00612.2001

Bell PG, Furber MJ, Van Someren KA, Anton-Solanas A, Swart J (2017) The Physiological Profile of a Multiple Tour de France Winning Cyclist. Med Sci Sports Exerc. 49:115-123 https://doi.org/10.1249/mss.0000000000001068

Bogaerts K, Notebaert K, Van Diest I, Devriese S, De Peuter S, Van den Bergh O (2005) Accuracy of respiratory symptom perception in different affective contexts. J Psychosom Res. 58:537-543 https://doi.org/10.1016/j.jpsychores.2004.12.005

Bonini M et al. (2020) Minimal clinically important difference for asthma endpoints: an expert consensus report. Eur Respir Rev. 29:190137 https://doi.org/10.1183/16000617.0137-2019

Bonini M, Lapucci G, Petrelli G, Todaro A, Pamich T, Rasi G, Bonini S (2007) Predictive value of allergy and pulmonary function tests for the diagnosis of asthma in elite athletes. Allergy. 62:1166-1170 https://doi.org/10.1111/j.1398-9995.2007.01503.x

Bougault V, Odashiro P, Turmel J, Orain M, Laviolette M, Joubert P, Boulet LP (2018) Changes in airway inflammation and remodelling in swimmers after quitting sport competition. Clin Exp Allergy. 48:1748-1751 https://doi.org/10.1111/cea.13257

Dempsey JA, La Gerche A, Hull JH (2020) Is the Healthy Respiratory System Built Just Right, Overbuilt or Underbuilt to Meet the Demands Imposed by Exercise? J Appl Physiol. https://doi.org/10.1152/japplphysiol.00444.2020

Derchak PA, Stager JM, Tanner DA, Chapman RF (2000) Expiratory flow limitation confounds ventilatory response during exercise in athletes. Med Sci Sports Exerc. 32:1873-1879 https://doi.org/10.1097/00005768-200011000-00009

Dickinson JW, Whyte G, McConnell A, Harries M (2005) Impact of changes in the IOC-MC asthma criteria: a British perspective. Thorax. 60:629-632 https://doi.org/10.1136/thx.2004.037499

Dickinson JW, Whyte GP, McConnell AK, Harries MG (2006a) Screening elite winter athletes for exercise induced asthma: a comparison of three challenge methods. Br J Sports Med. 40:179-182 https://dx.doi.org/10.1136%2Fbjsm.2005.022764

Dickinson JW, Whyte GP, McConnell AK, Nevill AM, Harries MG (2006b) Mid-expiratory flow versus FEV1 measurements in the diagnosis of exercise induced asthma in elite athletes. Thorax. 61:111-114 https://dx.doi.org/10.1136%2Fthx.2005.046615

Dominelli PB et al. (2017) Effects of respiratory muscle work on respiratory and locomotor blood flow during exercise. Exp Physiol. 102:1535-1547 https://doi.org/10.1113/ep086566

Dominelli PB, Katayama K, Vermeulen TD, Stuckless TJR, Brown CV, Foster GE, Sheel AW (2019) Work of breathing influences muscle sympathetic nerve activity during semi-recumbent cycle exercise. Acta Physiol. 225:e13212 https://doi.org/10.1111/apha.13212

Dweik RA et al. (2011) An official ATS clinical practice guideline: interpretation of exhaled nitric oxide levels (FENO) for clinical applications. Am J Respir Crit Care Med. 184:602-615 https://dx.doi.org/10.1164%2Frccm.9120-11ST

Fernández-García B, Pérez-Landaluce J, Rodríguez-Alonso M, Terrados N (2000) Intensity of exercise during road race pro-cycling competition. Med Sci Sports Exerc. 32:1002-1006 https://doi.org/10.1097/00005768-200005000-00019

Foster GE et al. (2014) Pulmonary mechanics and gas exchange during exercise in Kenyan distance runners. Med Sci Sports Exerc. 46:702-710 https://doi.org/10.1249/mss.0000000000000161

Fullagar HHK, Skorski S, Duffield R, Hammes D, Coutts AJ, Meyer T (2015) Sleep and athletic performance: the effects of sleep loss on exercise performance, and physiological and cognitive responses to exercise. Sports Med. 45:161-186 https://doi.org/10.1007/s40279-014-0260-0

Gift AG (1989) Validation of a vertical visual analogue scale as a measure of clinical dyspnea. Rehabil Nurs. 14:323-325 https://doi.org/10.1002/j.2048-7940.1989.tb01129.x

Graham BL et al. (2019) Standardization of spirometry 2019 update. An official American thoracic society and European respiratory society technical statement. Am J Respir Crit Care Med. 200:e70-e88 https://doi.org/10.1164/rccm.201908-1590ST

Guenette JA, Witt JD, McKenzie DC, Road JD, Sheel AW (2007) Respiratory mechanics during exercise in endurance-trained men and women. J Physiol. 581:1309-1322 https://doi.org/10.1113/jphysiol.2006.126466

Harms CA, Wetter TJ, St. Croix CM, Pegelow DF, Dempsey JA (2000) Effects of respiratory muscle work on exercise performance. J Appl Physiol. 89:131-138 https://doi.org/10.1152/jappl.2000.89.1.131

Helenius I, Rytilä P, Sarna S, Lumme A, Helenius M, Remes V, Haahtela T (2002) Effect of continuing or finishing high-level sports on airway inflammation, bronchial hyperresponsiveness, and asthma: a 5-year prospective follow-up study of 42 highly trained swimmers. J Allergy Clin Immunol. 109:962-968 https://doi.org/10.1067/mai.2002.124769a

Holmberg HC, Rosdahl H, Svedenhag J (2007) Lung function, arterial saturation and oxygen uptake in elite cross country skiers: influence of exercise mode. Scandanavian J Med Sci Sports. 17:437-444 https://doi.org/10.1111/j.1600-0838.2006.00592.x

Hull JH, Dickinson JW, Jackson AR (2017) Cough in exercise and athletes. Pulm Pharmacol Ther. 47:49-55 https://doi.org/10.1080/15438629609512061

Irwin RS et al. (2006) Diagnosis and management of cough executive summary: ACCP evidence-based clinical practice guidelines. Chest. 129:1S-23S https://doi.org/10.1378/chest.129.1_suppl.1s

Kennedy MD, Davidson WJ, Wong LE, Traves SL, Leigh R, Eves ND (2016) Airway inflammation, cough and athlete quality of life in elite female cross-country skiers: A longitudinal study. Scandanavian J Med Sci Sports. 26:835-842 https://doi.org/10.1111/sms.12527

Kippelen P, Anderson SD (2012) Airway injury during high-level exercise. Br J Sports Med. 46:385 http://dx.doi.org/10.1136/bjsports-2011-090819

Knöpfli BH, Luke-Zeitoun M, von Duvillard SP, Burki A, Bachlechner C, Keller H (2007) High incidence of exercise-induced bronchoconstriction in triathletes of the Swiss national team. Br J Sports Med. 41:486 https://doi.org/10.1136/bjsm.2006.030569

Laveneziana P et al. (2019) ERS statement on respiratory muscle testing at rest and during exercise. Eur Respir J. 53:1801214 https://doi.org/10.1183/13993003.01214-2018

Le Meur Y et al. (2013) Evidence of parasympathetic hyperactivity in functionally overreached athletes. Med Sci Sports Exerc. 45:2061-2071 https://doi.org/10.1249/mss.0b013e3182980125

Lee KK, Matos S, Evans DH, White P, Pavord ID, Birring SS (2013) A longitudinal assessment of acute cough. Am J Respir Crit Care Med. 187:991-997 https://doi.org/10.1164/rccm.201209-1686oc

Lucía A, Hoyos J, Santalla A, Earnest C, Chicharro JL (2003) Tour de France versus Vuelta a Espana: which is harder? Med Sci Sports Exerc. 35:872-878 https://doi.org/10.1249/01.mss.0000064999.82036.b4

Lucia A, Hoyos J, Santalla A, PÉRez M, Chicharro JL (2002) Kinetics of VO2 in professional cyclists. Med Sci Sports Exerc. 34:320-325 https://doi.org/10.1097/00005768-200202000-00021

Medelli J, Lounana J, Messan F, Menuet JJ, Petitjean M (2006) Testing of pulmonary function in a professional cycling team. J Sports Med Phys Fit. 46:298

Moreira A, Delgado L, Carlsen K-H (2011) Exercise-induced asthma: why is it so frequent in Olympic athletes? Expert Rev Respir Med. 5:1-3 https://doi.org/10.1586/ers.10.88

Niinimaa V, Cole P, Mintz S, Shephard RJ (1980) The switching point from nasal to oronasal breathing. Respir Physiol. 42:61-71 https://doi.org/10.1016/0034-5687(80)90104-8

Parsons JP et al. (2013) An official American Thoracic Society clinical practice guideline: exercise-induced bronchoconstriction. Am J Respir Crit Care Med. 187:1016-1027 https://doi.org/10.1164/rccm.201303-0437ST

Pichot V et al. (2002) Autonomic adaptations to intensive and overload training periods: a laboratory study. Med Sci Sports Exerc. 34:1660-1666 https://doi.org/10.1097/00005768-200210000-00019

Price OJ, Ansley L, Bikov A, Hull JH (2016a) The role of impulse oscillometry in detecting airway dysfunction in athletes. J Asthma. 53:62-68 10.3109/02770903.2015.1063647

Price OJ, Ansley L, Menzies-Gow A, Cullinan P, Hull JH (2013) Airway dysfunction in elite athletes-an occupational lung disease? Allergy. 68:1343-1352 https://doi.org/10.1111/all.12265

Price OJ, Hull JH (2014) Asthma in elite athletes: Who cares? Clin Pulm Med. 21:68-75 https://10.1097/CPM.0000000000000030

Price OJ, Hull JH, Ansley L (2014a) Advances in the diagnosis of exercise-induced bronchoconstriction. Expert Rev Respir Med. 8:209-220 https://doi.org/10.1586/17476348.2014.890517

Price OJ, Hull JH, Ansley L, Thomas M, Eyles C (2016b) Exercise-induced bronchoconstriction in athletes - A qualitative assessment of symptom perception. Respir Med. 120:36-43 https://doi.org/10.1016/j.rmed.2016.09.017

Price OJ, Hull JH, Backer V, Hostrup M, Ansley L (2014b) The impact of exercise-induced bronchoconstriction on athletic performance: a systematic review. Sports Med. 44:1749-1761 https://doi.org/10.1007/s40279-014-0238-y

Quanjer PH et al. (2012) Multi-ethnic reference values for spirometry for the 3–95-yr age range: the global lung function 2012 equations. Eur Respir J. 40:1324 10.1183/09031936.00080312

Romer LM, Lovering AT, Haverkamp HC, Pegelow DF, Dempsey JA (2006) Effect of inspiratory muscle work on peripheral fatigue of locomotor muscles in healthy humans. J Physiol. 571:425-439 https://doi.org/10.1113/jphysiol.2005.099697

Romer LM, Polkey MI (2008) Exercise-induced respiratory muscle fatigue: implications for performance. J Appl Physiol. 104:879-888 https://doi.org/10.1152/japplphysiol.01157.2007

Rundell KW (2004) Pulmonary function decay in women ice hockey players: is there a relationship to ice rink air quality? Inhal Toxicol. 16:117-123 https://doi.org/10.1080/08958370490270918

Rundell KW, Anderson SD, Sue-Chu M, Bougault V, Boulet LP (2015) Air quality and temperature effects on exercise-induced bronchoconstriction. Compr Physiol. 5:579-610 https://doi.org/10.1002/cphy.c130013

Rundell KW, Im J, Mayers LB, Wilber RL, Szmedra L, Schmitz HR (2001) Self-reported symptoms and exercise-induced asthma in the elite athlete. Med Sci Sports Exerc. 33:208-213 https://doi.org/10.1097/00005768-200102000-00006

Rundell KW, Smoliga JM, Bougault V (2018) Exercise-induced bronchoconstriction and the air we breathe. Immunol Allergy Clin. 38:183-204 https://doi.org/10.1016/j.iac.2018.01.009

Sanders D, Heijboer M (2019) Physical demands and power profile of different stage types within a cycling grand tour. Eur J Sport Sci. 19:736-744 https://doi.org/10.1080/17461391.2018.1554706

Seiler S, Haugen O, Kuffel E (2007) Autonomic recovery after exercise in trained athletes: intensity and duration effects. Med Sci Sports Exerc. 39:1366-1373 https://doi.org/10.1249/mss.0b013e318060f17d

Sheel AW, Derchak PA, Morgan BJ, Pegelow DF, Jacques AJ, Dempsey JA (2001) Fatiguing inspiratory muscle work causes reflex reduction in resting leg blood flow in humans. J Physiol. 537:277-289 https://doi.org/10.1111/j.1469-7793.2001.0277k.x

Simpson AJ, Romer LM, Kippelen P (2015) Self-reported symptoms after induced and inhibited bronchoconstriction in athletes. Med Sci Sports Exerc. 47:2005 https://dx.doi.org/10.1249%2FMSS.0000000000000646

Simpson AJ, Romer LM, Kippelen P (2017) Exercise-induced dehydration alters pulmonary function but does not modify airway responsiveness to dry air in athletes with mild asthma. J Appl Physiol. 122:1329-1335 https://dx.doi.org/10.1152%2Fjapplphysiol.01114.2016

Stensrud T et al. (2020) Lung function and oxygen saturation after participation in Norseman Xtreme Triathlon. Scandanavian J Med Sci Sports. 30:1008-1016 https://doi.org/10.1111/sms.13651

Tammie RE, David TM, Brian S, Warren M, Robert TW (2007) Fluid and Food Intake During Professional Men's and Women's Road-Cycling Tours. Int J Sports Physiol Perform. 2:58-71 https://doi.org/10.1123/ijspp.2.1.58

Tiller NB, Turner LA, Taylor BJ (2019) Pulmonary and respiratory muscle function in response to 10 marathons in 10 days. Eur J Appl Physiol. 119:509-518 https://doi.org/10.1007/s00421-018-4037-2

Vergès S, Devouassoux G, Flore P, Rossini E, Fior-Gozlan M, Levy P, Wuyam B (2005) Bronchial hyperresponsiveness, airway inflammation, and airflow limitation in endurance athletes. Chest. 127:1935-1941 https://doi.org/10.1378/chest.127.6.1935

Vergès S, Flore P, Blanchi MPR, Wuyam B (2004) A 10-year follow-up study of pulmonary function in symptomatic elite cross-country skiers–athletes and bronchial dysfunctions. Scandanavian J Med Sci Sports. 14:381-387 https://10.1111/j.1600-0838.2004.00383.x

Vernillo G, Rinaldo N, Giorgi A, Esposito F, Trabucchi P, Millet GP, Schena F (2015) Changes in lung function during an extreme mountain ultramarathon. Scandanavian J Med Sci Sports. 25:e374-e380 https://doi.org/10.1111/sms.12325

Widdicombe J, Fontana G, Gibson P (2009) Workshop–cough: exercise, speech and music. Pulm Pharmacol Ther. 22:143-147 https://doi.org/10.1016/j.pupt.2008.12.009