SUPPLEMENTARY FILES

BTS Clinical Statement for the Assessment and Management of Respiratory Problems in Athletic Individuals

TABLE S1 - Considerations and recommendations when performing physiological investigations in athletes.

Physiological test	Considerations	Recommendations
SPIROMETRY AND FLOW VOLUME LOOPS		
Use of Peak flow	• Peak flow can be reduced by conditions mimicking EIB / asthma (e.g. BPD, EILO - see later) and fatigue.	Do not rely on peak flow as a sole indicator of AFO or as a key physiological marker for EIB during an exercise test.
Interpretation; application of reference ranges	• Some athletes appear to have supra-normal indices (e.g. swimmers and rowers) but athletic training does not change spirometry indices. • The shape of the maximial flow-volume curve may provide insight regarding the cause of exertional breathing difficulties (e.g. oscillations indicating potential large airway collapse)	Apply usual reference ranges when interpreting spirometry in athletic individuals.
Interpretation; diagnosis of airflow obstruction	• Do not use a fixed cut off for the FEV_1/FVC ratio for defining AFO. Use the lower limit of normal (LLN) defined as -1.64 Z scores (the	Beware diagnosing asthma based on spirometry showing a supra-normal FVC and normal FEV1 in large athletes and evaluate BDR and other markers of

	lower 5th centile); this is now provided by most modern spirometer devices and based on population reference values. ● Some athletes may have larger lung volume in relation to airway calibre, which may be normal. A reduced FEV_1/FVC ratio should always be followed with BD reversibility testing.	airway disease (e.g. FeNO).
Interpretation; evaluation of inspiratory flow	● Highly effort dependent and found to be neither specific nor sensitive for EILO but may raise suspicion of this problem.	Changes in inspiratory flow may indicate upper airway problem but can also indicate poor effort or dysfunctional breathing and thus should be interpreted with caution.
Use of bronchodilator reversibility	● May be of value even if the FEV_1/FVC ratio is normal, but difficult to interpret implications of results and better to use challenge test if possible. ● Use standard guideline protocols and interpretative strategy.[101]	Important in establishing evidence of reversible AFO and apply and interpret as per general population.
FeNO MEASUREMENT		
Pre-test considerations	● Foods high in Nitrates, e.g. beetroot shots (often taken by athletes) can impact measurement significantly.[102] ● Avoid exercise prior to testing and perform FeNO before any spirometry measurement.	Consider specific factors that may impact result.
Interpretation	● Apply standard reference values.[103]	Interpret as per normal reference ranges.

BRONCHOPROVOCATION / EXERCISE-INDUCED BRONCHOCONSTRICTION TESTING		
Selection of test **Direct** - Methacholine Histamine **Indirect** - Eucapnic Voluntary Hyperventilation Lab or field-based exercise Mannitol	● Direct challenge testing involves using a stimulus that has a direct action on airway smooth muscle. These are generally more sensitive but less specific for EIB. i.e. more likely to be positive in the absence of EIB.[9] ● Indirect challenge testing involves using a stimulus that acts on intermediary cells which cause an inflammatory cascade which then acts on airway smooth muscle. These are generally more specific than direct challenges. i.e. more likely to detect EIB that will respond to treatment.[104] ● Use cut-off values as per recognized guidelines.	Test selection is often driven by local access and availability but are important means of ensuring a robust diagnosis. Indirect bronchoprovocation testing methodology is favoured when used to assess EIB. Always consider the pre-test clinical probability of a given diagnosis prior to interpreting a bronchoprovocation test.
Exercise testing for EIB	● A field based EIB test should last approx. 6 minutes of vigorous exercise (i.e. heart rate >80% of predicted maximum heart rate) with FEV1 fall >10% post exercise from baseline, indicating a positive result.[13] ● When performing laboratory based exercise tests, the ambient conditions should be sufficiently cold and dry (<50% humidity at 23℃, if temperature is below 10℃ air will be sufficiently dry).[13]	Exercise testing for EIB, whilst intuitive, can be difficult to perform due to stringent protocol requirements. A negative test can be falsely reassuring. If an athlete is symptomatic during an exercise test and there is no change in spirometry, this should prompt consideration of other diagnoses.

Pre-test considerations	● The accuracy of any test for EIB may be influenced by pre-attendance exercise (cf the refractory period) and intake of caffeine.	Follow the current ERS guidelines[105] for pre-testing preparation.
CARDIOPULMONARY EXERCISE TESTING		
Test Performance	● An incremental ramp CPET protocol is available in many hospital settings now. Breath-by-breath data allows evaluation of factors limiting exercise tolerance. ● The typical protocols employed (i.e. slow incremental ramp) and face mask (i.e. with increased humidity from airway expiratory moisture) mean that this is a specific but insensitive means of detecting EIB. ● Evaluate breathing pattern and audible wheeze / stridor. ● Can help identify deconditioning; i.e. in context of otherwise normal response patterns.	CPET has most value in the assessment of athletic individuals reporting profound symptoms. It is a poor test to detect EIB, although if an athlete's symptoms are precipitated post CPET, then normal spirometry can be helpful in ruling out airways disease.
Interpretation	● CPET is a complex test which requires detailed interpretation of various measurements and specialist knowledge to identify dysfunctional breathing[56] [57] and other features of ventilatory limitation (e.g. expiratory flow limitation) ● Well trained athletes will often exhibit evidence of ventilatory limitation which is a normal response in this type of subject. i.e.	In athletic individuals, CPET should be interpreted by experienced individuals. Level of training, prior athletic capability should be considered.

	because of an athletically / highly adapted cardiac system. ● Well trained athletes may have abnormal resting ECG findings.[8]	
Specific and relevant findings	● Exercise induced arterial hypoxaemia (EIAH) may be seen in some athletes and is defined as a reduction in the blood oxygen level (i.e. SpO2 of <95%, or 3–4% fall from rest) during exercise.[106]	EIAH should be interpreted with caution when using pulse oximetry and ideally hypoxaemia should be confirmed with arterial blood gas.

Defn. of abbreviations: AFO – airflow obstruction; CLE – Continuous Laryngoscopy during exercise; EIB – Exercise induced bronchoconstriction; EILO – Exercise induced laryngeal obstruction FeNO – Fraction of exhaled nitric oxide; FEV_1 – Forced expiratory volume in 1 second; FVC – Forced vital capacity; LLN – lower limit of normal.

TABLE S2 - Clinical features of a breathing pattern disorder

Objective Assessment	Normal	BPD
Symptoms	Normal breathlessness on exertion	Disproportionate breathlessness, difficulty taking deep breaths, chest discomfort and tightness
Route of air entry	Nose breathing, gradually transitioning to mouth breathing during exercise	Tendency for excessive mouth breathing
Breathing pattern	Diaphragmatic / abdominal – leading from lower and lateral rib cage	Apical – leading from upper chest Asynchrony between upper and lower chest movement
Respiratory rate	10-12 breaths per minute (adolescents & adults) – proportionally increased with exercise	Respiratory rate exceeds metabolic demands
Posture	Upright, head and neck in alignment with body with appropriate sport specific adaptations	Slumped posture, rounded shoulders with head forwards
Respiration	Quiet & relaxed, with increasing loudness with intensity	Excessively audible or noisy breathing
Accessory muscle use	Increasing proportionally with exercise intensity	Excessive

TABLE S3 – Key anti-doping considerations in the treatment of respiratory illness

- An athlete's health should never be jeopardized by withholding medication in an emergency for fear of incurring an anti-doping rule violation.
- In acute emergency situations (e.g. an asthma attack), proceed to deliver standard care but document all clinical examination findings, including symptoms and peak flow readings. A retroactive TUE application (see TUE) will be considered following treatment with this information.
- The most commonly used treatments for respiratory care (e.g. inhaled corticosteroid and antibiotics) are not prohibited.
- Some asthma inhalers can be used to pre-determined limits, i.e. there is a threshold. This includes salbutamol: maximum 1600 micrograms (i.e. 16 puffs of a standard 100 MDI) over 24 hours in divided doses ***but*** not to exceed 6~~8~~00 micrograms over 8~~12~~ hours starting from any dose; formoterol: maximum delivered dose of 54 micrograms (i.e. 9 puffs of a standard 200/6 strength turbohaler) over 24 hours; salmeterol: maximum 200 micrograms over 24 hours; and vilanterol: maximum 25 micrograms over 24 hours. This ruling can change and to check for the most up-to-date information see www.wada-ama.org/en/prohibited-list.
- A number of beta-2 agonists are included on the Prohibited List requiring a TUE for their use (e.g. Terbutaline). The Prohibited List is updated on an annual basis and it is thus recommended that athletes and clinicians consult www.globaldro.com +/- the relevant national anti-doping organisation for further advice.
- Oral corticosteroids are prohibited in-competition and as such require a TUE if used.
- Administration of salbutamol via nebulization is likely to result in urinary levels of salbutamol exceeding the threshold limit and thus use of salbutamol with a nebulizer requires a TUE.

TABLE S4 –FOCUS FOR FUTURE RESEARCH

Diagnosis and assessment

- Evaluation and validation of simple, widely accessible, non-invasive tools (e.g. sound-based / mobile phone based systems) to determine cause of wheeze and breathlessness
- Validation of specific tools (e.g. athlete-specific questionnaires) for surveillance of respiratory health issues
- Improved characterisation of respiratory tract 'infections' with point-of-care microbial diagnostics
- Development of widely available and cost-effective tools to detect and characterise BPD

Treatment

- Multi-centre, randomised-controlled intervention studies in EILO and BPD
- Evaluation of novel medications that may protect and improve airway surface health in athletes
- Evaluation of treatments / strategies to optimise immune function and other potential factors in athletes deemed susceptible to respiratory tract infection

Other / general respiratory health protection

- Mechanistic work to understand risk of airway 'injury' in some endurance athletes and longitudinal studies to evaluate risk factors for development of respiratory issues during an athletic career
- Improved characterisation of environmental impact on airway health in athletes; e.g. impact of pollution, thermal change.
- International registry studies to improve insight regarding prevalence of respiratory issues.