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EDITORIAL

Limitation to muscular activity in chronic obstructive pulmonary disease

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The constellation of laboured breathing, fixed inflated lungs that neither fill nor empty properly was first described in 1685 by WILLIS [1]. *Post mortem* examination revealed that these lungs failed to deflate on opening of the chest [2], and the term emphysema was introduced [3]. Chronic bronchitis was viewed as a separate entity occasionally coexisting with emphysema. Airway obstruction was recognised as the key feature of emphysema and chronic bronchitis at the end of the 1950s. This was formally acknowledged at a Ciba Guest Symposium held in 1959 [4] and endorsed by the American Thoracic Society in 1962 [5]. The functional consequences of airway obstruction progress from a reduced capacity to breathe and exchange respiratory gases, to respiratory failure, pulmonary hypertension, right heart failure and premature death. A reduction in the forced expiratory volume in one second (FEV1) and the FEV1/vital capacity ratio, and failure to improve with treatment are the diagnostic features of what is known today as chronic obstructive pulmonary disease (COPD).

In this issue of the *European Respiratory Journal*, CORONELL *et al.* [6] report that COPD patients have a reduced ability to sustain repetitive muscular contractions and that their muscles fatigue rapidly. The reduced ability to perform activities of everyday life with comfort is usually attributed to dyspnoea and breathlessness, resulting from patients' reduced capacity to breathe and exchange gas. In 1877, Paul Bert convincingly demonstrated that hypoxaemia caused the profound fatigue experienced at high altitude. Although hypoxaemia is a contributing factor to fatigue, it is modest, if not absent, in most COPD patients. Fatigue might simply be a function of muscle weakness. In clinical practice, little consideration is given to the muscle mass available for activation. Formal measurements of muscle strength, used as an indicator of muscle mass, frequently disclose muscle weakness in COPD patients.

Neuromuscular fatigue refers to the relationship between the motor command and the power output of the muscle. Fatigue is present when the motor command increases to sustain the same power output over time. Fatigue is peripheral when the responsiveness of the muscle declines due to reduced muscular perfusion, hypoxaemia, anaemia or dysfunction in any intramuscular process. Fatigue is central when the responsiveness of the alpha motor neurons decline due to efferent activity from higher central neurons and afferent activity from within the muscle projecting on the alpha motor neurons. When a muscle reaches maximum power output or sustains a given power output to limitation, both are perceptually expressed through the sense of effort. When the effort becomes intolerable, power generation is terminated and the discomfort promptly recedes. At the point of power failure, distinction is attempted between fatigue and limiting processes, such as reduced perfusion, reduced oxygen delivery or failure to maintain acid base balance.

A central motor command activates the alpha motor neurons causing membrane depolarisation and calcium release from the sarcoplasmic reticulum activating cross bridging of actin myosin. Muscle shortens and tension is developed. High energy phosphates (ATP) are essential for maintaining membrane charge (1%), calcium release and reuptake (20%) and cross bridging of actin myosin (~80%). The rate of ATP production is high by anaerobic metabolism but can only be sustained for seconds; is lower by aerobic oxidation of carbohydrates but can be sustained for hours until stores are depleted; and is even lower by aerobic oxidation of fats but can be sustained for days to weeks. Individuals with exceptional endurance display slow muscle fibres, high capillary density, high mitochondrial density and high aerobic enzyme content, while individuals with exceptional strength display fast muscle fibres, low capillary and mitochondrial density, and low aerobic enzyme content. Oxidative phosphorylation is supported by ventilation, gas exchange and circulation.

A comprehensive framework for assessment of disease severity based on impairment, disability and handicap has evolved under the guidance of the World Health Organization [7]. This might be useful to adopt in COPD where the severity of disease would be assessed in terms of its impact on the capacity to exercise, as is used in cardiovascular disease (New York Heart Association class I–IV). The capacity to exercise, measured by an incremental exercise test on a cycle ergometer, is related to sex, age and height through differences in muscle mass, which is seldom acknowledged [8]. Measurements of strength of peripheral and respiratory muscles, spirometry, maximal flow volume loop and carbon dioxide diffusing capacity of the lung are obtained before a standardised incremental exercise test to symptom-limited capacity, with symptom rating of leg effort and dyspnoea. When the effort becomes intolerable exercise is terminated.

Our understanding of chronic obstructive pulmonary disease continues to evolve and so should our approach to management. In chronic obstructive pulmonary disease, exercise is limited by a reduced capacity to breathe, a reduced capacity to exchange gas, and a reduced capacity to generate and sustain power output. Muscle weakness contributes substantially to the capacity to exercise. Overly simplistic views of impairment in chronic obstructive pulmonary disease confined to ventilatory and gas exchange capacity are no longer adequate.

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