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Editorial Overview: Current Opinion in Exercise Physiology

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Muscular exercise demands an exquisite integration of physiologic function to mobilize the mass transport of oxygen from the atmosphere to the muscles and carbon dioxide back to the atmosphere. These processes ultimately power the transport of the smallest of molecules across the thinnest of membranes: A single proton transported across the 75 angstrom-thick inner mitochondrial membrane provides the motive force to “evade the decay to equilibrium” [1] and maintain organismal homeostasis. The wide ranging bodily processes that integrate to support oxidative phosphorylation are key to the ability to meet the exercise stressor in a steady-state.

Regular exercise not only helps to optimize these transport processes and increase performance, but its profound and beneficial influence upon essentially all tissues of the body is increasingly clear – even on those tissues seemingly uninvolved in oxygen transport or muscle contraction. This is nowhere more obvious than in physical inactivity, where deranged cardiovascular, metabolic and neurologic function are among ailments of inactivity-induced chronic disease. The broad and deep impact of acute and chronic exercise across biological scales has led to substantial efforts to better understand how regular exercise leads to improved physical function, health and longevity.

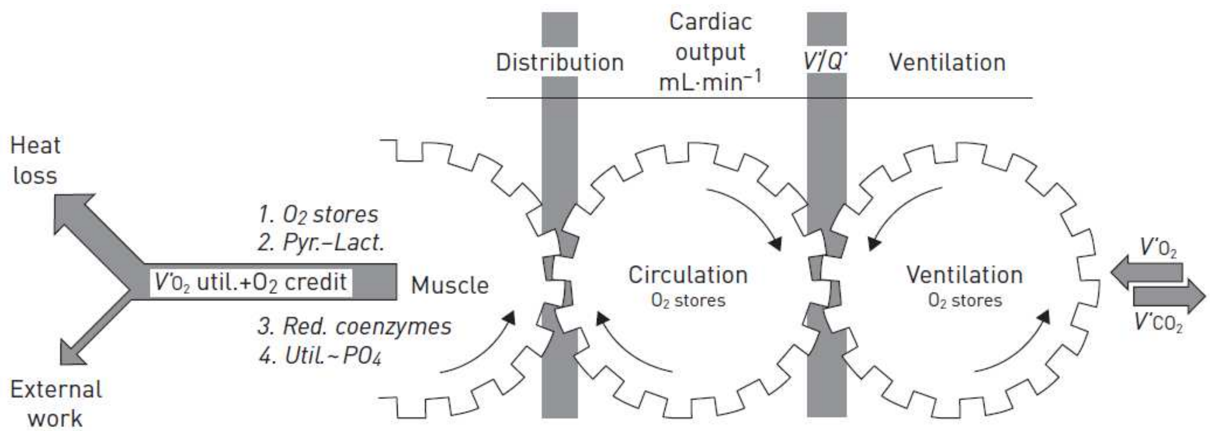

Figure. The interaction of physiological mechanisms during exercise based on the classic 1967 conceptualization of Wasserman et al. [2]. The ability to perform exercise is dependent on the performance of a number of linked systems. $\dot{V}O_2$: oxygen uptake; $\dot{V}/\dot{Q}$: ventilation/perfusion ratio; $\dot{V}CO_2$: carbon dioxide production. Pyr.: pyrate; lact.: lactate; util.: utilization. Reproduced from [2] with permission from the publisher.

The collection of articles of the review series featured in Current Opinion in Physiology – Vol. 10 focuses on the thoughts and guidance from outstanding exercise physiologists across the globe on recent hot topics within the field. Fifty two years after Karlman Wasserman offered us a conceptual framework for the field of exercise physiology, in the form of pulmonary, circulatory and muscular “gears” (Figure) [2], the discipline has expanded to show us the influences of e.g. sex, age, maturation, nutrition, circadian rhythms, tissue crosstalk, on the wide gamut of physiologic systems. This series was conceived with this expansive, and expanding, field in mind, while providing topical reviews on the core exercise physiological principles described within Wasserman's gears. The initial focus is on how the body responds to the immediate challenge of acute exercise. Subsequent contributions highlight mechanisms of adaptation when exercise becomes chronic e.g. resistance or endurance training, potential exercise biomarkers and the influence of tissue crosstalk on the healthful adaptive response to regular exercise. The series concludes with the influence of modulators such as sex, age, nutrition, heat stress, altitude, or time-of-day on physiologic responses to exercise.

Thus, this series begins at the mitochondrial level with **Petrick and Holloway** discussing how mitochondria regulate lipid and carbohydrate metabolism during activity. **Drake and Yan** propose that mitochondrial quality control is mediated within local spatial domains in exercising muscle. While **Porcelli et al.** detail the oxygen transport and utilization limitations of mitochondrial myopathy patients.

At the muscular level, **Sundberg and Fitts** explore the mechanisms behind reduction in muscle contractile power associated with fatiguing high intensity exercise, and propose non-mitochondrial energy conversion pathways resulting in inorganic phosphate and hydrogen ion accumulation as a direct cause. Fatiguing events in isolated muscle contractions, however, do not necessarily extrapolate exercise performance limitation. For this, **Amann and Weavil** discuss current data showing that fatigue is not isolated to muscles of locomotion during whole body exercise, but also occurs centrally and in non-locomotor muscles.

The challenge that acute exercise poses to the cardiovascular system is largely how to deliver blood flow to the appropriate tissues and, within them, microvascular units, to match supply to regional demand. **Gliemann et al.** detail recent findings on the acute blood flow response to exercise and particularly on the mechanistic control of vasodilation in skeletal muscle. **Viana and Fisher** provide evidence that targeting group III and IV skeletal muscle afferents may be effective in improving the matching between oxygen supply and demand across the spectrum of cardiovascular disease. The remarkably similar response of the cardiorespiratory system to exercise across vertebrate species, despite large differences in anatomy, is detailed by **Wang et al**.

The capacity of the respiratory system has long been considered more than adequate to meet the gas exchange needs for exercise in healthy populations. However, **Philips and Stickland** suggest further investigations are needed into recently described limitations of gas exchange, ventilation, and respiratory muscle function in healthy individuals during exercise. **Welch et al.** review the evidence that respiratory muscle mechanics, energetics, and force generation may limit exercise tolerance. The upper airways typically do not comprise a major source of resistance in the respiratory system. However, **Price et al.** highlight recent discoveries using continuous laryngoscopy about the response of the upper and large central airways during exercise. **Ward** delves into ventilatory control during exercise emphasizing the methodological and theoretical challenges about the regulation of arterial PCO_2 during exercise, which still remain unanswered.

The plasticity of human physiology in response to regular exercise training underlies its wide ranging health benefits. Recent advances in strength and endurance training are provided in the first two reviews of those focusing on training adaptations. **Morton et al.** present the evidence for optimizing resistance training programs for either strength or muscle hypertrophy, and **Gibala et al.** address the differential skeletal muscle and cardiovascular responses to interval training. Specific effects of training within cardiac and skeletal muscle are then explored. **Deschenes** examines the adaptations to both the pre- and post-synaptic regions of the neuromuscular junction and suggests that the magnitude of response may differ depending on the type of training. The mechanisms mediating the muscle angiogenic response to exercise training are discussed by **Kissane and Egginton** who also suggest that accounting for the spatial heterogeneity in muscle may lead to better design of training programs in both healthy and recovering populations. **Hill** challenges the common use of reductionism and promotes the use of relational biology to investigate how metabolic stressors, such as exercise, lead to cardiac remodeling.

A major impact of the aging process is the decline in ability of tissues to respond as they once did to a training stimulus. **Laurin et al.** focus on endurance exercise training and its benefits in maintaining muscle mass and function in aging populations. How aerobic exercise protects vascular function in aging populations is the subject of the review by **Craighead et al.,** which also provides information on how healthy lifestyle choices can provide similar benefits.

The benefits of exercise on the whole body are now known to be much more than just the sum of the effects on the individual systems. Much of this is likely due to communication among physiological systems. Skeletal muscle releases numerous factors into the blood stream during exercise, which can be taken up and/or sensed by other tissues. **Ellingsgaard et al.** detail the current status of one of the earliest known of these myokines, IL-6, which may play a role in exercise-induced fat loss, appetite suppression and immune function. MicroRNAs are another factor that can be released into the blood to potentially modulate distant tissues. The exercise response and biomarker potential of circulating microRNAs are examined by **Sapp and Hagberg**, who find there is still much to be determined in this nascent field.

The scope of knowledge of biological or environmental or modulators exercise responses continues to expand rapidly. The impact of heat exchange during exercise on aging populations is described by **Meade et al.** where fitness, disease, hydration, and acclimation status all play major roles. Deficits in exercise performance at high altitude are the focus of **Grocott et al.** who show that losses of muscle mass and mitochondrial content and function, in addition to the classically described oxygen delivery limitations, each contribute to reductions in maximal oxygen uptake and performance at extreme altitudes.

One of the few biological processes that rivals exercise in its breadth of affected physiological systems is the molecular clock that controls circadian oscillations in genes and function in nearly every cell in the body. **Wolff and Esser** suggest that specific timing of exercise interventions to optimize metabolic and hormone responses may offer a promising approach to improve outcomes in both patients and healthy subjects such as athletes.

Nutrition, supplementation and recovery strategies are key to optimizing exercise performance and adaptation. **De Souza et al.** provide two reviews on the potential outcomes of improper nutrition and recovery strategies in athletes, first describing current knowledge of the female athlete triad and its relationship with energy availability assessments, and second, delivering an update on the newly established male athlete triad. **Burke** reviews the wide ranging literature on common supplements and calls for additional rigorous studies such that athletes and coaches can make informed decisions about their use. **Dearlove et al.** focus on ketone bodies and discuss the potential of properly designed ketone supplements for improving performance. Finally, the crucial role of exercise recovery strategies are reviewed by **Peake,** who outlines the current use of nutritional, physical, and sleep methodologies.

This issue provides a glimpse into the current state of exercise physiology research around the world. A critical component of this review series is the inclusion of the current challenges in the field and the expert guidance on how to overcome them. A common theme is to include more integrative approaches to better understand the complex interactions that occur in response to exercise. Another common theme as study design develops to appropriately include more females in exercise research, is the identification of sex differences in the acute and chronic exercise response across wide ranging physiologic systems. We hope that the reader will agree that this forward-looking collection of accessible and topical reviews emphasizes that it is an exciting time to be an exercise physiologist!

References

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