

## Respiratory muscle work and oxidative stress in the elderly: impact on blood flow and fatigue.

### SPECIFIC AIMS

Compared to young individuals, older subjects are characterized by substantially increased respiratory muscle work ( $W_r$ ), and elevated oxidative stress - especially during exercise (14, 18, 22). Considering these observations, two specific findings in young healthy humans form the rationale for this proposed project: First, relieving much of  $W_r$  during cycling exercise via ventilatory assist increases leg blood flow ( $Q_{leg}$ ) and  $O_2$  delivery (11, 12). Second, end-exercise locomotor muscle fatigue is significantly ameliorated by relieving much of  $W_r$  (1, 7) and oxidative stress (16) normally incurred during sustained endurance exercise.

Based on these findings, we propose the following specific aims:

#### 1. What is the impact of $W_r$ and oxidative stress on muscle fatigue and exercise tolerance in the elderly?

- a) Determine the effects of constant-load cycling exercise-induced  $W_r$  on locomotor muscle fatigue, systemic oxidative stress, and exercise tolerance.

Hypothesis: Relieving much of the exercise-induced  $W_r$  via pressure support ventilation will significantly reduce the development of quadriceps fatigue and attenuate systemic oxidative stress resulting in a significantly greater improvement in endurance time to exhaustion in the elderly compared to young individuals.

- b) Determine the effects of cycling exercise-induced systemic oxidative stress on locomotor muscle fatigue and exercise tolerance.

Hypothesis: Attenuating exercise-induced oxidative stress via intravenous antioxidant infusion will reduce the development of quadriceps fatigue and improve endurance time to exhaustion significantly more in the elderly compared to young individuals.

#### 2. Is the age-related impact of $W_r$ and oxidative stress on locomotor muscle fatigue mediated by $Q_{leg}$ ?

- a) Determine the impact of exercise-induced  $W_r$  on  $Q_{leg}$  and the associated impact on locomotor muscle oxidative stress generation.

Hypothesis: Relieving much of the exercise-induced  $W_r$  via pressure support ventilation plus heliox will increase  $Q_{leg}$  and attenuate locomotor muscle oxidative stress generation significantly more in the elderly compared to young individuals.

- b) Determine the impact of exercise-induced systemic oxidative stress on  $Q_{leg}$ .

Hypothesis: Attenuating exercise-induced oxidative stress via intravenous antioxidant infusion will increase  $Q_{leg}$  significantly more in the elderly compared to young individuals.