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Guest Editorial

Exercise and Cystic Fibrosis: The Search for a Therapeutic Optimum

There can be no more compelling goal for pediatric health care professionals than to restore the chronically ill child or teenager to as full and healthy a lifestyle as possible. Inevitably, this task involves some form of exercise program since normal childhood and adolescence are developmental stages in humans (and other mammals) characterized by vigorous, spontaneous, and frequent physical activity.[1,2] For children with cystic fibrosis, a number of pioneering investigators have established that exercise interventions can be safe and even therapeutic.[3,4] However, as pointed out by Nikolaizik et al.[5] in this issue of the journal, few cystic fibrosis centers offer a structured exercise intervention for their patients.

The Nikolaizik article highlights two fundamental problems of current research and clinical approaches to exercise as therapy in children and thus may help us find some solutions. The first issue is directly addressed by Nikolaizik and coauthors. Are exercise tests (and accompanying markers of functional capability) that have been developed for healthy subjects suitable for testing children with chronic diseases? Specifically, can such tests and physiological markers be used to gauge levels of exercise that are safe and beneficial in the patient with cystic fibrosis?

Nikolaizik et al. focused on the so-called Conconi[6] method of determining the lactate or anaerobic threshold during exercise from the heart rate signal alone, rather than the more arduous measurements of gas exchange and/or blood lactate. While serious physiological and methodological questions surround this approach, the Conconi method has gained widespread use (particularly in Europe) because of its seeming simplicity. Nikolaizik and coauthors convincingly demonstrate that the heart rate method substantially overestimated the work rate above which lactic acidosis ensues. As a consequence, exercise prescriptions for cystic fibrosis patients based on the heart rate method would impose too heavy a metabolic load and could lead to noncompliance and/or possibly dangerous levels of hypoxemia and metabolic acidosis.

This is an important observation. In the presence of physiological impairment (in this case, the lung and/or right-sided heart disease of cystic fibrosis) one cannot assume that existing exercise testing is valid. Indeed, the paradigm of modern exercise testing, designed largely as a tool to identify individuals with exceptionally *high* limits of functional capability (e.g., child athletes), may not be useful to define disabilities in children whose limits are likely to be *low*. At the very least, the Nikolaizik article challenges us to rethink the way in which we use exercise testing diagnostically. Perhaps the time has come for a new set of exercise testing paradigms designed specifically for children with disease and disability.

An issue of equal, or perhaps even greater, importance is implicitly raised by the Nikolaizik article. Exactly what is it about exercise that may benefit the child or adolescent (or adult) with chronic disease? This is a tricky question, and to research why ''exercise is good for you'' may seem naive and simplistic. However, we know that physical activity can enhance mucus clearance,[7] attenuate insulin resistance,[8] promote tissue growth factor gene expression like insulin-like growth factor-I[9] and fibroblast growth factor,[10] and alter the neuroendocrine control of metabolism.[11] This suggests the possibility of a more profound and important role for exercise as therapy. Indeed, when applied correctly, the exercise prescription may yet prove to be an elegant and natural way to stimulate and/or promote the expression of beneficial genes.

The challenge of understanding how (and whether) exercise interventions may work to promote health in patients with chronic diseases like cystic fibrosis is particularly daunting. It is likely that in children with underlying physiological constraints, the boundary between therapeutic effects of exercise (characterized, perhaps, by tissue expression of growth factors) and harmful effects (characterized by tissue cytokines and neuroendocrine stress responses) is less distinct than in healthy children. A normally health-promoting exercise could, in a child with chronic lung or heart disease, become deleterious if, for example, oxygen delivery to tissues was sufficiently impaired.

Articles like those of Nikolaizik et al. will hopefully encourage efforts to develop innovative approaches toward understanding the basic mechanisms and conditions that render exercise interventions truly therapeutic in children with chronic diseases. As caregivers of some of the most physically active humans, pediatricians and

other child health care professionals should accept this task quite comfortably.

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