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Authors

Moser, Chuanpit
Nussbaum, Eliezer
Cooper, Dan M

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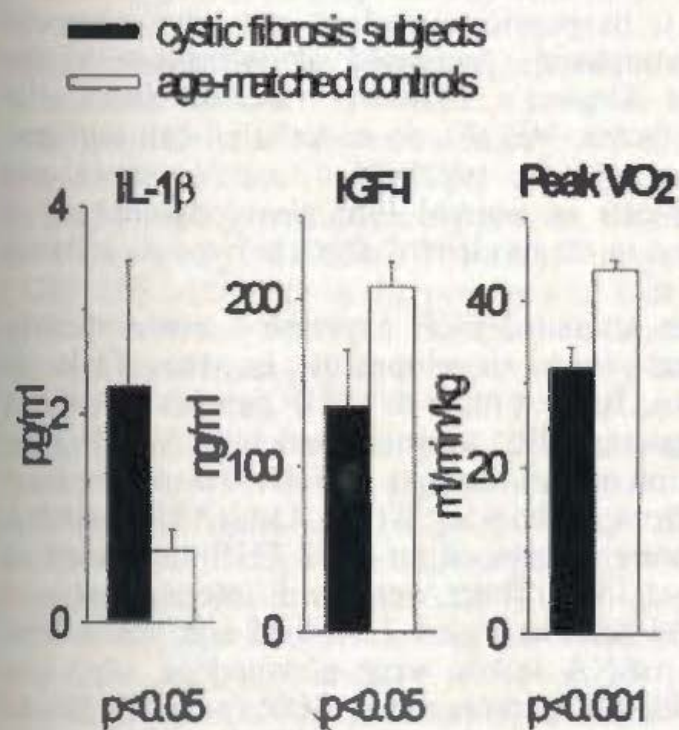
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Circulating IL-1 β , IGF-I, and Fitness in Cystic Fibrosis

Chuanpit Moser, Eliezer Nussbaum, Dan M Cooper, Pediatrics, University of California, Irvine, Irvine, CA, Pediatrics, Miller Children's at Long Beach Memorial Medical Center, Long Beach, CA

Fitness is associated with longevity in CF (Nixon et al. *NEJM* 327:1785, 1992). However, the optimal level of physical activity in children and adolescents with CF is difficult to evaluate because the underlying disease is associated with increased basal energy expenditure, hypoxemia, malnutrition, and inflammation, all of which promote tissue catabolism even at rest. We hypothesized that anabolic

function would be depressed, circulating inflammatory cytokines elevated, and fitness reduced in CF subjects compared with healthy controls. A total of 7 CF subjects (age range 7-13 years) were compared with 22 age-matched healthy controls. Fitness was assessed by peak oxygen uptake (VO_2) from standard progressive exercise cycle ergometry. Insulin-like growth factor-I (IGF-I), an anabolic mediator, and the proinflammatory cytokine interleukin-1 β (IL-1 β), a catabolic mediator, were measured by ELISA. Blood samples were obtained under resting conditions. As shown in the Figure, IL-1 β was higher, and IGF-I and fitness were significantly lower in the CF subjects compared with controls. In addition, IGF-I was significantly correlated with fitness expressed either as peak VO_2 /kg ($r=0.59$) or percent predicted ($r=0.65$). We speculate that the increase in circulating IL-1 β in CF may result from hypoxia and/or chronic pulmonary inflammation and antagonize IGF-I. This leads to the development of a catabolic state and reduced muscle mass. Consequently, peak VO_2 is impaired as IGF-I is correlated with relative muscle mass (Eliakim et



al., *JCEM* 81:3986, 1996). Measuring indexes of catabolic and anabolic activity along with traditional measurements of fitness may help optimize the exercise prescription for CF patients. It may also distinguish those patients most likely to benefit by exercise from those who may be adversely affected by any increase in energy expenditure. Finally, this approach could provide a mechanistic basis for understanding the effects of exercise interventions in children with CF.

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