SYMPOSIUM

Introduction: Physiology, Pathophysiology, and Genetics of Body Weight/Adiposity Regulation

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The prevalence of obesity in the United States and other "Westernized" countries has reached epidemic proportions. As reported by scientists at the Centers for Disease Control and Prevention (6), in 2000, 38.8 million American adults were considered obese, having a body mass index of 30 or higher. [Body mass index is calculated as weight in kilograms divided by height in meters squared (i.e., kg/m^2)]. This represents 19.8% of U.S. adults, a 61% increase since 1991. An additional 72 million are overweight, with body mass indices between 25 and 29.9 (6). The fact that obesity is a major risk factor for numerous diseases including diabetes and cardiovascular disease makes it imperative that we have a better understanding of the peripheral and central factors that normally regulate body weight and adiposity. It was with this goal in mind that the Society for Experimental Biology and Medicine organized a symposium focusing on this topic.[2] The resulting group of five papers represents contributions from four of the symposium participants (1,2,4,7) plus an invited minireview on adipocyte differentiation (3).

The review by Havel (4) emphasizes that there are both short and long-term regulators of energy balance. The short-term signals derive primarily from the gastrointestinal tract and mediate cessation of meals; while the long term signals, such as insulin and leptin exert their effects on both energy intake and energy expenditure. These long-term effects involve a dynamic regulatory process that attempts to match energy intake to energy expenditure. Schwartz (7) describes the evidence for the involvement of specific hypothalamic neurons and neuropeptides in this regulation.

Also involved in this regulation are the adipocytes as well as other peripheral tissues. Collins and her colleagues (1) summarize data demonstrating the importance of adrenergic pathways and brown adipocytes in regulatory energy expenditure. In addition, they discuss the potential role that members of the uncoupling protein family may play in fuel metabolism, pointing out the uncertainty regarding the physiological function of these proteins in cells other than brown adipocytes. The complex nature of adipocytes is further demonstrated in the minireview by Gregoire (3) who describes the highly controlled process whereby preadipocytes proliferate and differentiate into white adipocytes that not only store fuel but that also secrete proteins that in turn, mediate numerous physiological and pathological processes.

Moving from the pathways that play a role in the normal regulation of energy balance, Froguel and Boutin (2) consider the genetics that may underlie the dysfunction of these pathways and the development of obesity. While it is recognized that the increased incidence of obesity in the United States reflects life-style changes, it is also acknowledged that the susceptibility for obesity has a genetic component. The Froguel and Boutin review of human genetic data points to several such susceptibility genes but also indicates that we are still in the initial stages of this line of inquiry (2).

As emphasized by the group of contributors, our understanding of the pathways regulating body weight and adiposity and how they become dysfunctional relies on a variety of experimental approaches ranging from the molecular to the integrative. Knopp (5) has previously pointed out that this multidisciplinary approach, which is fostered by the Society of Experimental Biology and Medicine, is indeed a powerful one as it facilitates the integration of

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basic science with medicine and holds the promise for answering major medical questions.

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