



Obesity and heart disease

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It is well established that obese individuals are at an increased risk of developing cardiovascular disease. As a result, the dramatic increase in the incidence of obesity worldwide will have a profound impact on the severity and incidence of heart disease. Indeed, as a risk factor for heart disease, obesity in the 21st century is what tobacco was in the 20th century. In tackling the problem of obesity, it is obviously important to try to decrease both the incidence and severity of obesity. In addition, it is also critical to gain a better understanding of how obesity contributes to the development of heart disease, and to develop and optimize treatments that lessen its impact on heart disease. Although patients with obesity have an increased risk for ischemic heart disease, a significant proportion of these patients will develop heart failure independent of ischemia. This edition of *Heart and Metabolism* addresses the important topic of obesity, highlighting the mechanistic links between obesity and heart disease, and therapeutic strategies for diagnosing and treating heart disease in the obese individual.

A number of direct changes to the myocardium can contribute to the development of cardiac dysfunction in the patient with obesity. These include a link between excessive rates of fatty acid β -oxidation in the heart and alterations in cardiac function. In the Basic Article, E. Dale Abel discusses the effects that obesity exerts directly on the alterations in fatty acid metabolism in the heart, which contributes to the development of insulin resistance. Potential mechanisms responsible for accelerated cardiac fatty acid oxidation rates in obesity are also discussed. This raises the possibility of targeting fatty acid metabolism

directly as an approach to treating heart disease in obesity.

Brown adipose tissue (BAT)* differs from white adipose tissue in that it is rich in mitochondria. Although long known to be important in metabolic and temperature control in rodents, the role of BAT in controlling metabolic rates in humans has not been obvious, because it was believed that BAT stores were very small in humans. However, the recent discovery that BAT activity can be detected in a substantial proportion of the adult population has generated a renewed interest in the study of this tissue. The New Therapeutic Approaches article by Peter Butler and colleagues also highlights the potential of stimulating BAT metabolism as a future therapeutic approach for treating obesity and insulin resistance. Measuring BAT content in humans has been difficult, but the Metabolic Imaging article by Kirsi Virtanen and Pirjo Nuutila provides some interesting data showing that positron emission tomography is a highly sensitive, non invasive tool for the in-vivo imaging of BAT in humans, providing unique information on the basic function and physiology of BAT.

Important BAT proteins involved in the control of metabolic rates are the mitochondrial uncoupling proteins (UCPs), which have long been known to control metabolic rates and body temperature in BAT of rodents. The UCPs dissipate the mitochondrial membrane potential, resulting in energy expenditure directly towards heat production as opposed to energy production. More recently, UCPs have emerged as important determinants of metabolic rate in humans. This not only occurs in BAT, but also via the expression of different UCP isoforms in other tissues, such as

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skeletal muscle. The Refresher Corner article by Frédéric Bouillaud provides an excellent review of the role of UCPs in physiology, and the recent interest in these proteins as potential targets in the treatment of obesity.

The contribution of obesity to cardiovascular disease necessitates early disease detection and prompt intervention in this high-risk group. However, as highlighted in the Case Report by Ian Webb and Michael Marber, accurate assessment of symptoms can be challenging at times, because of the presence of several comorbidities. An example of this complexity is presented in the case report of a patient with obesity who was under multidisciplinary care for symptoms of breathlessness; many of these issues arose in this patient. The Hot Topics article by Alda Huqi also reviews a number of clinical trials showing that most of the reduction in cardiovascular mortality and morbidity reported in recent years has been attributed to preventive measures, but that these same preventive

measures, when individually tested in high-risk subgroups of patients, often fail to improve clinical outcomes. The Main Clinical Article by Jennifer Logue and Naveed Sattar also highlights the complexity of the relationship between obesity and heart disease. Although an association between obesity and increased heart disease is well established, there exists an “obesity paradox” in which there is a greater survival among obese patients with cardiac failure. The authors describe the phenomenon and discuss possible factors that may be responsible for this apparent paradox.

With the epidemic of obesity in our society, this edition of *Heart and Metabolism* is a timely publication, with a number of articles discussing ways in which to “Tackle Obesity”. Failure to address these important issues will almost assuredly contribute to an increase in the incidence of heart disease in the world.

*see glossary for definition of this term.