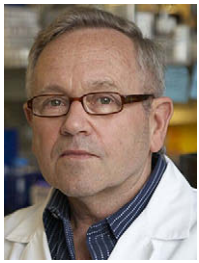
Foreword



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In this second issue on obesity, the emphasis is more on the control of feeding behavior and the peripheral metabolism by the hypothalamus and management of the disorder.

Energy stores in various compartments of the body are regulated quite tightly by the hypothalamus. Although energy homeostasis is controlled mainly by neuronal circuits in the hypothalamus and brainstem, reward and motivational aspects of eating behavior are controlled by neurons in limbic regions and the cerebral cortex. The first article in this issue, by Ahima and Antwi, outlines these processes and suggests quite rationally their importance in the search for therapeutic agents for the obesity epidemic.

Buettner and Camacho, on the other hand, describe the hypothalamic control of glucose and lipid homeostasis itself. Clearly the hypothalamus affects appetite and satiety. During the last decade, we have come to understand the critical role of the hypothalamus in nutrient homeostasis. The hypothalamus senses fasting glucose levels and, by affecting liver glucose output, it controls fasting blood glucose levels. In the postprandial state, it similarly affects glucose levels and is capable of inducing conversion of glucose into storage forms (eg, glycogen and lipids). Recent research has also shown that most organs involved in nutrient homeostasis, such as the pancreas, liver, muscles, and fat, are indeed under its control.

In a very telling article by Lara-Castro and Garvey, there is a description of the intramyocellular (IMCL) and intrahepatocellular lipid accumulation that is commonly seen in obese individuals with elements of the metabolic syndrome and those with type 2 diabetes. This IMCL contributes to the insulin resistance seen in these conditions. Importantly, IMCL may also be seen in athletes where it is not associated with insulin resistance and here the intracellular locus and size of these lipid droplets may differ. Furthermore, the lipid droplets in athletes demonstrate increased availability of the free fatty acids required to meet the high oxidative requirements during exercise.

In the article by Hsiao, Metz, Singh, and Roth, an exciting new area of research is described: the relationship between the flora of the gut and human physiology—in this case obesity. It appears that certain gut flora affect nutrient uptake and homeostasis both by affecting digestion of nutrients and by releasing certain peptides that interact with gut receptors. This area of research opens a whole new concept of gut flora–gastrointestinal tract interactions and has many ramifications for other disorders besides obesity.

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One of the most difficult topics in obesity is the issue of dietary management, both for reducing weight and for weight maintenance. Dubnov-Raz and Berry discuss this difficult topic by comparing the various well-studied diets that involve low calorie, low fat, and many fad diets. Though some diets, such as Atkins, low calorie, Mediterranean, and low glycemic index, have proven relatively effective, the most critical issue remains compliance (ie, the human element).

O'Gorman and Krook discuss the importance of exercise in the management of obesity and prevention of many of the complications associated with excess weight. There are apparently genetic determinants for the ability to respond to excess weight. There are a number of genetic and phenotypic effects of exercise, including changes in mitochondrial metabolism and switching of muscle fiber types. These and other changes are important for improvements not just in weight reduction, but also in reducing the negative effects on the cardiovascular system that are associated with obesity.

As compliance of lifestyle modification is very important in managing obesity, Van Dorsten and Lindley pursue the issue of behavioral therapy in the lifestyle management of obesity, both for weight reduction and maintenance. Both the dietary and exercise components of therapy require cognitive-behavioral elements to implement lifestyle changes, thereby enhancing its effectiveness and avoiding relapses.

There is a large amount of interest in using medications to treat obesity. On the one hand, lifestyle intervention alone has been largely unsuccessful in reversing the obesity epidemic. On the other hand, bariatric surgery is reserved for morbid obesity and moderate obesity with comorbidities. As described in the article by Bray, there are currently two drugs approved for treating obesity: sibutramine, an appetite suppressant, and orlistat, which interferes with fat digestion and absorption. Both are successful in helping produce weight reduction, but both have side-effects. Cannabinoid receptor-1 antagonists such as rimonobant are being testing in clinical trials and may be useful in the future for moderate weight reduction, if the side-effect profile is limited. Of note, the use of this drug is already approved in many countries of the European Union.

Smith, Schauer, and Nguyen cover the very important topic of bariatric surgery. Over the past decade, the techniques have evolved, and the morbidity and mortality of the procedures have been reduced dramatically, so that the value of this approach is now widely accepted for morbidly obese individuals (body mass index [BMI] > 40) and obese individuals (BMI > 35) who have comorbid diseases such as diabetes. Interestingly, there is now interest in using these techniques for treating patients who have uncontrolled type 2 diabetes as their primary disorder with mild obesity (BMI 28-35). While the first indications remain obesity, the more recent studies suggest that new indications such as diabetes may become realistic in the future once more studies have been presented.

Once again, Dr. Karnieli has produced an issue of high quality and of extreme interest to the medical community. Well done!

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