Preface

Obesity

The articles that have been chosen for this issue represent clinical aspects of this very important disorder. Obesity, as everyone knows, has become an epidemic, not just in North America, but worldwide. The epidemic of obesity is also driving the marked increase in type 2 diabetes worldwide. While obesity is easily recognizable clinically and readily measurable in the United States, a feature that is not well recognized is the central adiposity that maybe the only or main feature in South East Asian communities, many of whom are highly represented in the United States. Thus, often, we as clinicians may not be screening for the obesity-related abnormalities that represent the metabolic syndrome, and therefore, preventative or therapeutic modalities are introduced very late in the disease process.

The first article describes the Metabolic Syndrome specifically. The Metabolic Syndrome includes obesity, hypertension, hyperlipidemia, and glucose intolerance, has insulin resistance as the underlying etiology, and is commonly seen in patients with type 2 diabetes. As described in this article by Gallagher, LeRoith, and Karnieli, it is extremely common in both developed countries as well as in third-world countries and is associated with visceral adiposity. While the exact definitions of the metabolic syndrome differ slightly between various organizational and governing bodies, its existence and its relationship to type 2 diabetes are unequivocal. The article also presents information on how insulin resistance is caused by obesity and how the insulin resistance causes the hypertension, hyperlipidemia, and glucose intolerance.

Gerald Reaven was one of the first investigators who described the Metabolic Syndrome (which he originally named “Syndrome X”); here he describes the relationship between obesity and cardiovascular disease. He initially presents the relationship between abdominal obesity and reduced insulin-mediated glucose uptake into muscle. This resultant insulin resistance and hyperinsulinemia lead to increased risk factors for cardiovascular disease. Today this cardio-metabolic syndrome is so common that major efforts are underway to attempt to reverse the abnormality, since heart attacks and strokes are the major causes of the high mortality rates in type 2 diabetic patients.
Obesity and dyslipidemia is another complication that is commonly appreciated in the medical community. The cardiovascular risk associated with obesity is mostly predicted by the dyslipidemia, characterized by increased triglyceride levels, decreased high-density lipoproteins levels, and a shift in low-density lipoproteins (LDL) to a more pro-atherogenic composition (small, dense LDL). These features are covered in the article by Franssen, Monajemi, Stroes, and Kastelein. They describe how the classic concept of insulin resistance, lipolysis, with excess free fatty acid (FFA) release leading to hypertriglyceridemia is still the central theme.

Obesity-related hypertension has many etiologies, as outlined by Kurukulasuriya, Stas, Lastra, Manrique, and Sowers. These include the well-known causes such as insulin resistance, activation of the renin-angiotensinogen-aldosterone system with renal sodium retention, and the sympathetic nervous system. More recent studies have demonstrated that adipocytokines, FFAs, and other molecules may cause endothelial dysfunction. More recently the effect of sleep deprivation on obesity and therefore on hypertension has been described. While the causes are being investigated, the need for intensive anti-hypertensive therapy is primarily to prevent the cardiovascular and renal complications that result.

The relationship between obesity and cardiovascular disease is further explored in the article by Zalesin, Franklin, Miller, Peterson, and McCullough. They address the increased risk factors and increased cardiac disease in obese individuals that cause heart attacks, atrial fibrillation, and heart failure. Importantly, they describe the epidemic of obesity and the increased rates of hypertension, hyperlipidemia, and glucose intolerance in the pediatric population and the eventual increase in cardiovascular disease that is bound to result at younger ages.

One of the most difficult topics in obesity is the issue of dietary management for both reducing weight and weight maintenance. Dubnov-Raz and Berry discuss this difficult topic by comparing the various well-studied diets involving low-calorie, low-fat, and many fad diets. While some diets such as Atkins, low calorie, Mediterranean, and low glycemic index diets 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 the improvements, not just in weight reduction, but also in reducing the negative effects on the cardiovascular system, 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, for both weight reduction and maintenance. Both the dietary and the exercise components of therapy require cognitive-behavioral elements to implement the lifestyle changes, thereby enhancing their 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 is an appetite suppressant and orlistat 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 tested 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 was approved in many countries in the European Union, but subsequently removed due to excess side-effects.

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) with comorbid diseases such as diabetes. Interestingly, there is now interest in using these techniques for treating patients with uncontrolled type 2 diabetes as the primary disorder with mild obesity (BMI 28-35). While the first indication remains obesity, the more recent studies suggest that new indications such as diabetes may become realistic in the future once more studies have been presented.

These articles bring to the practicing physician knowledge about the basic pathophysiology and the clinical aspects of obesity, and we hope that the information is informative and practical.

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