Innovative Approach to Treatment of the Metabolic Syndrome

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In recent decades, we have seen a massive increase in the incidence of the metabolic syndrome. With the advent of bariatric surgery as the most effective method to achieve and maintain weight loss, multiple changes have also been discovered regarding its role in the management of diabetes and the metabolic syndrome. There is now extensive evidence to support metabolic surgery as a treatment not only for obesity but also for the well documented metabolic derangements that accompany it. The site of nutrient delivery in the gastrointestinal tract, malabsorption, and gut hormone secretion are all believed to play important roles in the proposed mechanism of action of metabolic surgery. Although the mechanisms of the long-term remission of diabetes and other obesity-associated co-morbidities are still being outlined, novel techniques and surgical innovations have provided very promising results in select groups of patients. This chapter deals with the history of metabolic surgery and its effects on diabetes and the metabolic syndrome. An overview of several hypotheses and theories behind the surgically induced changes that may lead to sustained remission of this disease is given, along with a discussion of the ongoing trials, to create a better understanding of the future role of surgery in the management of this patient population.

### 10.1 Background

The sky-rocketing rise in morbid obesity and associated complications in the United States is alarming and is a well-recognized problem worldwide [1]. The constellations of conditions associated with morbid obesity are numerous and include high blood pressure, dyslipidemia, insulin resistance, and visceral adiposity, and, combined, they lead to the metabolic syndrome. This syndrome is proven to be a risk factor for development of cardiovascular disease. The presence of insulin resistance in patients with metabolic syndrome confers an increased risk for type-2 diabetes, further increasing the risk for cardiovascular disease [2]. Obesity is a modifiable component of this syndrome and therefore the primary target for intervention [3, 4]. This intervention has traditionally been medical; however, with increasing surgical expertise in bariatric procedures, surgery has taken on a pivotal role in the management of the obese patient. Lifestyle modifications have been recommended as first-line therapy for weight reduction, resulting in lower serum cholesterol and triglyceride levels, higher serum HDL cholesterol, lower blood pressure and glucose levels, and reduced insulin resistance [3]. Pharmacological agents that treat specific components of the metabolic syndrome have also been successful in selective patients. These include statins, antihypertensive drugs, anti-platelet therapy, anti-obesity agents (such as lipase inhibitors and appetite suppressants), and insulin sensitizers or hypoglycemic agents when diabetes ensues. These therapies have proven to play important roles in the treatment of this disease. However, in the majority of obese patients with metabolic syndrome, medical therapy has not been sufficient as a long-term treatment to achieve sustained weight loss and glucose control [5]. In recent years, surgery has emerged as a promising alternative therapy for these morbidly obese patients with poor response to less invasive intervention. Gastric bypass surgery and other associated procedures have been proven to facilitate weight loss and ameliorate or resolve conditions associated with obesity, particularly type-2 diabetes mellitus [6–8]. Complete resolution of diabetes can be achieved not only in the morbidly obese but also in the semi-obese patient following bariatric surgery. This chapter provides an overview of the benefits of surgery as therapy for the metabolic changes associated with obesity, diabetes, and the metabolic syndrome.

### 10.2 Diabetes and the Metabolic Syndrome

#### 10.2.1 Public Health and Economic Crisis

Diabetes is the fifth leading cause of death in the United States [9]. There are approximately 20 million people in the United States (7% of the population) who have diabetes. In 2005, one and a half million new cases of diabetes were diagnosed in people 20 years or older [10]. It is of even more concern that, despite a decrease in the death rate related to heart disease, stroke, and cancer, the death rate due to diabetes has increased by 45% during the past 20 years [9]. It is projected that by 2012, the diabetic population will be an estimated 22.7 million in the United States and 226 million outside of the US [11]. Type-2 diabetes mellitus (T2DM) is estimated to constitute up to 90% of all diabetes cases [12]. Diabetes is now the most costly disease in the United States. In 2002, diabetes was accountable for cost amounting to 138 billion dollars between medical expenses and lost wages and productivity. By 2020, the overall cost associated with DM is expected to be close to 200 billion dollars per year [11].

#### 10.2.2 Success and Failure of Medical Management of Diabetes

Insulin resistance is central to the pathophysiology of T2DM. In its earlier phase, insulin levels rise to counter-