In today’s society with the escalating levels of obesity, diabetes, and cardiovascular disease, the metabolic syndrome is receiving considerable attention and is the subject of much controversy. Greater insight into the mechanism(s) behind the syndrome may improve our understanding of how to prevent and best manage this complex condition.

Insulin-mediated glucose disposal varies at least sixfold in apparently healthy individuals. The adverse effect of decreases in the level of physical fitness on insulin sensitivity is comparable to the untoward impact of excess adiposity, with each accounting for approximately 25% of the variability of insulin action. It is the loss of insulin sensitivity that explains why obese individuals are more likely to develop cardiovascular disease, but not all overweight/obese individuals are insulin resistant. At a clinical level, it is important to identify those overweight individuals who are also insulin resistant and to initiate the most intensive therapeutic effort in this subgroup. Finally, it appears that the adverse impact of overall obesity, as estimated by body mass index, is comparable to that of abdominal obesity, as quantified by waist circumference.

The alarming and still increasing prevalence of obesity and associated cardiovascular risk raises much concern. The increase in cardiovascular risk depends to a significant extent on the changes in lipid profiles as observed in obesity. These changes are decreased high-density lipoprotein cholesterol and increased triglyceride levels. Much effort has already been expended into the elucidation of the mechanisms behind these obesity-associated lipid changes. Insulin resistance certainly plays a central role and, in addition, both hormonal and neurologic pathways have recently been found to play an important role. This article focuses on the mechanisms involved in the development of the proatherogenic lipid changes associated with obesity.

Hypertension and obesity are major components of the cardiometabolic syndrome and are both on the rise worldwide, with enormous consequences.
to global health and the economy. The relationship between hypertension and obesity is multifaceted; the etiology is complex and it is not well elucidated. This article reviews the current knowledge on obesity-related hypertension. Further understanding of the underlying mechanisms of this epidemic will be important in devising future treatment avenues.

**Impact of Obesity on Cardiovascular Disease**

Kerstyn C. Zalesin, Barry A. Franklin, Wendy M. Miller, Eric D. Peterson, and Peter A. McCullough

The epidemiology of cardiovascular disease risk factors is changing rapidly with the obesity pandemic. Obesity is independently associated with the risks for coronary heart disease, atrial fibrillation, and heart failure. Intra-abdominal obesity is also unique as a cardiovascular risk state in that it contributes to or directly causes most other modifiable risk factors, namely, hypertension, dysmetabolic syndrome, and type 2 diabetes mellitus. Obesity can also exacerbate cardiovascular disease through a variety of mechanisms including systemic inflammation, hypercoagulability, and activation of the sympathetic and reninangiotensin systems. Thus, weight reduction is a key strategy for simultaneous improvement in global cardiovascular risk, with anticipated improvements in survival and quality of life.

**The Dietary Treatment of Obesity**

Gal Dubnov-Raz and Elliot M. Berry

Dietary modulation is an essential part of weight loss and maintaining its reduction. Although simple in behavioral terms (eat less, exercise more), the tremendous difficulty of weight loss and maintenance has inspired many different diet regimens, in search of an easier, more efficient way to lose weight. Contemporary issues in this matter are the composition of diets (low fat versus low carbohydrate), the choice of carbohydrate (the glycemic index), and the role of calcium and dairy products. This article discusses the scientific evidence of the various dietary manipulations for weight loss and the challenges of maintaining a reduced obese state.

**Exercise and the Treatment of Diabetes and Obesity**

Donal J. O’Gorman and Anna Krook

Lifestyle intervention programs encompassing exercise and healthy diets are an option for the treatment and management of obesity and type 2 diabetes and have long been known to exert beneficial effects on whole-body metabolism, in particular leading to enhanced insulin-sensitivity. Obesity is associated with increased risk of several illnesses and premature mortality. However, physical inactivity is itself associated with a number of similar risks, independent of body-mass index, and is an independent risk factor for more than 25 chronic diseases, including type 2 diabetes and cardiovascular disease. This article addresses the debate regarding the relative effects of physical exercise itself and the effect of exercise-induced weight loss.

**Cognitive and Behavioral Approaches in the Treatment of Obesity**

Brent Van Dorsten and Emily M. Lindley

Cognitive behavioral interventions have formed the cornerstone of obesity treatment for the past two decades. These techniques, often combined
with diet and exercise strategies, have been shown to produce weight losses of sufficient magnitude so as to reduce health risks. Though success in producing short-term weight loss is improving, many factors, including a metabolic energy gap, continue to challenge long-term weight maintenance results. This article reviews the unique influence of cognitive, behavioral, and metabolic factors on weight loss and weight-loss maintenance, and how future treatment packages might be modified to improve long-term weight loss outcomes.

**Medications for Weight Reduction**

George A. Bray

Only two drugs are currently approved for long-term use in the treatment of obesity, and four others for short-term use. Evaluating the risk-benefit profile is an essential first step. For individuals who have a low body mass index for whom the risk is small, the risk profile must make the drug acceptable for almost everyone. For higher-risk patients, such as those planning intestinal bypass or who have sleep apnea, a wider range of drugs may be considered. Obesity is a chronic disease that has many causes. Treatment is aimed at palliation—that is, producing and maintaining weight loss. Regardless of the primary site of action, the net effect must be a reduction in food intake or increase in energy expenditure.

**Surgical Approaches to the Treatment of Obesity: Bariatric Surgery**

Brian R. Smith, Phil Schauer, and Ninh T. Nguyen

As bariatric surgery for the treatment of morbid obesity enters its sixth decade, much has been and continues to be learned from the results of several key bariatric operations, particularly the Roux-en-Y gastric bypass. Because of the obesity epidemic and development of the laparoscopic approach, bariatric procedures have increased exponentially in the past decade and are now among the more commonly performed gastrointestinal operations. Emerging data support the role of bariatric surgery as an effective treatment for improvement or remission of type 2 diabetes, hypertension, dyslipidemia, and multiple other comorbid conditions that accompany obesity. The mechanisms involved in the remission of these conditions, however, remain poorly understood and constitute an exciting area of research. This article delineates the current types of bariatric surgery, their respective outcomes, and their impact on obesity-related medical comorbidities.