Obesity: Much Silence Makes a Mighty Noise

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In 2007, the majority of adults in the United States and many developed countries are overweight or obese. It is estimated that 1.6 billion adults worldwide are overweight (body mass index [BMI] > 25) and 400 million are obese (BMI > 30). Obesity puts millions of people at risk for serious medical conditions such as type 2 diabetes, cardiovascular disease, musculoskeletal disorders, sleep apnea, and some forms of cancer. Children are also increasingly overweight, with estimates as high as 20 million globally. Alarmingly, type 2 diabetes and other diseases thought to occur almost exclusively in adults are now prevalent in children. Furthermore, developing countries, which have dealt with the burden of infectious disease and undernutrition for decades are now facing an upsurge of obesity and its crippling health and economic consequences.

Why the silence about obesity until recently? Part of the problem stems from societal notions of what constitutes a “healthy weight” and whether obesity truly fits the definition of a “disease.” Attitudes about overweight and obesity range from acceptance of these conditions as indicative of prosperity and good health, to a negative perception of obese individuals as lacking self-control. Many governments and institutions still consider obesity a problem of personal choice that could be reversed simply by deciding to eat less and exercise more. In fact, some have questioned whether obesity is truly “epidemic.” Attitudes are changing, however, due to the rising incidences of diabetes and other debilitating diseases attributable to obesity. Moreover, the negative impact of obesity on health care budgets and various sectors of the economy is apparent. Scientific discoveries over the past decade have also enlightened us about the physiologic processes that control weight and metabolism. The drive to eat and store energy mainly as fat is fundamental for maintaining metabolic demands and ensuring survival. For human societies, the amount of available food was limited over several generations. As a result of improvements in agriculture which led to availability of cheap, palatable, and energy dense foods, overconsumption of food is now the norm, and this coupled with minimal physical activity has contributed prominently to the rising prevalence of obesity worldwide.

This special issue of GASTROENTEROLOGY presents a series of review articles on the epidemiology of obesity, pathophysiology, associated diseases, and management. The contributors are leading experts drawn from a variety of specialties, including epidemiology, endocrinology, metabolism, gastroenterology, behavioral science, and surgery. We emphasize that obesity is multidimensional and requires an integrated approach to understanding the extent of the problem, causation and health and socioeconomic consequences. Katherine Flegal (pages 2087–2102) reviews the epidemiology of obesity, highlighting controversies surrounding adiposity measurement, ethnic differences, childhood obesity, and diseases associated with obesity. Jeffrey Flier (pages 2103–2115) discusses how adipose tissue, the major energy store, regulates energy balance via hormones that act in the brain and peripheral organs. The discovery of leptin and its neuronal targets in the hypothalamus marked the beginning of concerted efforts to unravel how adipose tissue is coupled to feeding, energy expenditure, and regulation of hormones and immune and cardiovascular systems. Stephen Bloom (pages 2116–2130) reviews the role of gut hormones in appetite and weight regulation. Gut peptides serve as short-term signals to centers in the hindbrain to control meal size and timing, as well as gastrointestinal motility and secretions. Ultimately, these functions impact energy storage in adipose tissue. Daniel Drucker (pages 2131–2157) focuses on the biology of glucagon-like peptide (GLP)-1 and glucose-dependent insulintropic polypeptide (GIP), both secreted within minutes after eating. These incretin hormones facilitate the disposal of nutrients and have profound effects on glucose. Drugs based on potentiation of GLP-1 action

Abbreviations used in this paper: BMI, body mass index; GIP, glucose-dependent insulintropic polypeptide; GLP, glucagon-like peptide; mTOR, mammalian Target of Rapamycin.

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0016-5085/07/$32.00
doi:10.1053/j.gastro.2007.03.060
have been approved recently for the treatment of diabetes. Randy Seeley (pages 2158–2168) discusses how nutrients act as signals to the brain and peripheral organs to regulate feeding and metabolism. AMP-activated protein kinase plays a key role in integrating nutritional and hormonal signals and modulating feeding behavior and energy balance. The mammalian Target of Rapamycin (mTOR) also serves as a nutrient sensor in the hypothalamus. Steven Shoelson (pages 2169–2180) discusses the relationship between obesity and inflammation. Factors produced by inflammatory cells in adipose tissue have been linked to insulin resistance, and abnormal glucose and lipid metabolism in obesity. Daniel Rader (pages 2181–2190) reviews how obesity affects the lipid profile in a manner that may predispose to atherogenesis. The potential role of hyperinsulinemia in abnormal lipoprotein metabolism is discussed. Frank Anania (pages 2191–2207) discusses the pathophysiology of nonalcoholic fatty liver disease, in particular the role of insulin resistance and the relation to abnormal lipid and glucose metabolism. Putative mechanisms involved in hepatic inflammation and progression to fibrosis are discussed. Edward Giovannucci (pages 2208–2225) reviews the evidence for and against a connection between obesity and cancers of the colon, prostate and pancreas, and offers possible mechanisms based on animal experiments and epidemiological data. Thomas Wadden (pages 2226–2238) discusses the importance and strategies for lifestyle modification for the treatment of obesity. The efficacies of various diets, exercise and behavioral therapy are reviewed in detail. George Bray (pages 2239–2252) discusses the drug treatment of the overweight patient. Currently, only 2 drugs are approved for chronic treatment of obesity in the United States, and 3 in Europe. However, new drugs are being developed based on new insights into obesity pathophysiology. At present, bariatric surgery is the most effective treatment for attaining massive weight loss and ameliorating the complications of morbid obesity. Bruce Wolfe discusses surgical procedures for weight loss, criteria for patient selection, and outcomes. Lastly, the report of the AGA Institute Obesity Task Force, led by Lee Kaplan (pages 2272–2275) is presented.

Our hope is that this special issue will spur an interest in nutrition, metabolism, and obesity among physicians, health care providers, scientists, and the general public. A better understanding of pathophysiology provides a framework for evidence-based treatment of obesity. However, drugs and surgery alone cannot stem the tide of obesity. Ultimately, this requires changes in policies and societal practices pertaining to the “obesogenic” environment. Population-wide interventions that promote healthier foods, reduce consumption, and increase activity will lessen the burden of obesity and its comorbidities.