The causes, prevalence, and treatment of obesity revisited in 2009: what have we learned so far?1–3

Caroline M Apovian

ABSTRACT

Obesity is a chronic disease that is increasing in prevalence in the United States and worldwide and is often accompanied by multiple comorbidities that lead to type 2 diabetes and cardiovascular disease. In April 2009, the American Society for Nutrition hosted the symposium “An Integrative View of Obesity” at Experimental Biology 2009 in New Orleans, LA. The presentations addressed the causes of the obesity epidemic and notably discussed a combination of genetics, obesogenic environment, cultural and racial concerns, and treatment modalities based on what we have learned from research into the physiology and neuroendocrine regulation of appetite and satiety. The fat cell as an endocrine organ, in addition to contributions from the gut and pancreas, has helped us to understand the origins of this neuroendocrine regulation as a survival advantage in human ancestry, with obesogenic ramifications in today’s toxic food environment. Suggestions for the reversal of the obesity epidemic were offered, including public health campaigns, community and medical programs, and industry-supported change in our food supply, eating patterns, and lifestyle. Community-structured programs for exercise and work-related physical activity could also engage a healthier lifestyle into the typical day for the average American as well as for individuals in other countries. *Am J Clin Nutr* 2010; 91(suppl):277S–9S.

In this supplement to the Journal, we present the papers given at the Experimental Biology 2009 symposium entitled “An Integrative View of Obesity,” which was held in New Orleans, LA, last April. Due to the overwhelmingly positive response to the symposium, the American Society for Nutrition has formed a Research Interest Section on Obesity, which provides the potential for an annual symposium update on obesity starting with Experimental Biology 2010.

David Heber (1) began the symposium by addressing the interplay between physiology, human behavior, and the obesogenic environment and the resultant effect on the increasing prevalence of obesity; rates have increased acutely over the past 30 y and perhaps more gradually over the past 200 y due to the industrialization of our societies around the world. In fact, in the United States, the prevalence of extreme obesity has increased twice and 3 times as fast for body mass indexes (BMIs; in kg/m²) >40 and >50, respectively, compared with the prevalence of a BMI >30 between 2001 and 2005 (2). This highlights the tendency for some subpopulations to become severely obese in this environment, due to genetics, ethnicity, or cultural or psychological factors or a combination of all of these variables (3). Heber next addressed the issue of comorbidities related to obesity itself. There is a large body of current research that interweaves a chronic state of low-grade inflammation and the development of comorbidities as sequelae of obesity. Centering on the fat cell as an endocrine organ has led to the discovery of leptin (4), a potent regulator of energy balance, and paved the way for not only the adipose cell but also the gut and pancreas to be heralded as major players in energy regulation, appetite, and satiety in the brain (5–7). This has led researchers to investigate new pathways into neuroendocrine regulation in the hypothalamus and how genetics and genetic determinants of this regulation can play a role in the solution to the obesity problem (8, 9). Even though humans have developed a myriad of pathways over the millions of years that we have inhabited the planet, clearly not all humans are plagued with weight gain (10). Dissecting the differences between those of us who gain weight easily and those of us who don’t has proven to be a difficult task. In addition, it seems that, on a metabolic level, those who gain weight do not gain equally in terms of risk of cardiovascular disease (11), although it is true that cardiovascular risks intensify with higher degrees of obesity (12). In our recent study of subjects who underwent adipose tissue biopsy, we found that histologic findings of inflammation in fat, which was characterized by macrophage infiltration that congregates in a crownlike pattern, were associated with insulin resistance and systemic inflammation as well as vascular endothelial dysfunction. Past studies have suggested a correlation between abdominal obesity and increased disease risk; however, our study found that the effects of inflammation in fat were independent of BMI (11). This is another reason why BMI is not the most accurate predictor of risk, and perhaps in the future, adipose tissue biopsy can be a more useful tool to help assess cardiovascular risk due to obesity (13).

The next presentation, by Barry Popkin (14), outlined the American story in terms of a shifting BMI over the past 3 decades toward the upper end of the BMI distribution and then paralleled this increase with similar but delayed trends in other parts of the world. Although Popkin stressed that the highest BMIs (>50) are

1 From the Boston University School of Medicine, Boston, MA.
3 Address correspondence to CM Apovian, Boston University School of Medicine, 88 East Newton Street, Robinson Building, Suite 4400, Boston, MA 02118. E-mail: caroline.apovian@bmc.org.
First published online November 11, 2009; doi: 10.3945/ajcn.2009.28473A.
increasing exponentially in all age groups and sexes in the United States and worldwide, the largest increase has been in women and younger children. With these higher BMIs in children comes an increase in the demand for more-aggressive treatments for obesity, such as bariatric surgery in younger age groups (15, 16). In fact, in certain diverse urban populations in the United States, the prevalence of overweight adolescents is rising to an extent such that a relatively large proportion would qualify for weight loss surgery (17). Such surgery would serve as a stopgap to treat extreme obesity in younger age groups before comorbidity and higher risk occur (18–21); however, it is certainly not a solution to the problem. What has many researchers flummoxed is the degree to which some subgroups have escalated faster in terms of the higher ranges of BMI than other groups (22). This seems to suggest that there are genetic predispositions that are driving the dramatic weight gain in the current environment (23). However, supposition and correlations do not prove causation. Therefore, we must continue with research trials to review the evidence and dissect with precision what combination of factors has caused this alarming trend, particularly in certain subgroups of the world (24, 25).

George Blackburn anchored the symposium by discussing the state of our nation in the midst of an obesity epidemic and by calling for a shortening of the “energy gap” (26). The energy gap refers to an excess of kilocalories consumed per day in combination with a decrease in kilocalories expended, a situation that is responsible for the collective weight gain of the American population over the past several decades. The excess has been quantified as substantial (>400 kcal/d) (27, 28); however, data from 24-h dietary recalls (29) reveal that Americans admit to eating less than this excess amount of kilocalories per day. A total of almost 25% of all the energy consumed in the US population comes from nutrient-poor food groups, such as sweets and desserts. Americans do, however, admit to 7.1% of their energy intake coming from sugar-sweetened beverages, including soft drinks (29, 30). In response to these data, Blackburn called for several public health measures, including decreasing caloric intake, improving macronutrient content of diets, and increasing physical activity, to counteract this trend. There is no panacea coming soon from medicine or surgery in the form of a pill, device, or procedure that can undo the past 3 decades of poor nutrition and lack of physical activity.

Continuing with the trajectory of the past 30 y would result in 86% of Americans becoming overweight or obese by 2030, according to Wang et al (31), with 1 in 6 of every health care dollar being spent on obesity and its sequelae. Because 2030 is only a little over 20 y away, it seems that the idea of an economic shift needs to move beyond discussion into action, so that our lower socioeconomic classes can afford to buy more nutritious foods than chips and soda pop at the gas station (32, 33). The placement of high taxes on nutrient-poor foods, such as candy and sugar-sweetened beverages, as well as subsidies for fruit and vegetable farming, may put a dent in the energy gap that separates us “girthwise” from today and the 1960s (34–36). In addition, in response to the sedentary lifestyle of television watching and computer games, we need more outdoor activities for children and adolescents that would start in schools and extend throughout the typical childhood day (37, 38).

We may be able to connect the dots between Heber, Popkin, and Blackburn and by recognizing that certain groups of people seem to be gaining weight more easily. This is most notable in African American women and children and Hispanic women and children (22) and highlights ethnicity and sex as differential factors in the obesity epidemic. Therefore, studying genetics and culture could be beneficial in unfolding the cause or causes of weight gain in this particularly obesogenic environment. Because not all races, sexes, and cultures gain weight at the same rate (22), perhaps studying these differences can give us clues as to the causes of weight gain in our current world environment. What are the major reasons for worldwide weight gain? What is the effect of an increase in caloric intake or a decrease in physical activity? Could genetic variation plus caloric imbalance or a viral or bacterial infection be causing a change in energy balance via neuroendocrine control of appetite and satiety? Can we really blame it all on liquid calories (39)? However, even if we can pinpoint the increase in weight gain over time on the quantity and quality of food and drink we consume, some of us seem to be immune. Fat storage efficiency is not created equal. In fact, if we think beyond the “big 2” putative causes of obesity (excess calories and lack of exercise) as Keith et al (40) have done, there must be other potential reasons for the obesity epidemic to have skyrocketed out of the stratosphere. For example, Keith et al (40) have studied whether other factors, such as lack of sleep, the intrauterine environment, and a decrease in variability of ambient temperatures in combination with excess calories and a decrease in hard labor, may have been enough to explain our increases in adiposity (40). An investigation of these possibilities can help tease out the nuances of why our societies have expanded in girth over the past 3 decades, without a clear plateau in sight.

The changes in the environment that relate to physical activity and diet seem to have caused the obesity epidemic. The other side of the equation is the genetic makeup of humans, which has evolved over centuries and has caused the emergence of a “thrifty gene” (41). In short, the problem of obesity is multidimensional, and therefore the solution should tackle both genetics and the environment simultaneously (42).

Perhaps the most poignant reminder of the need to combat and find a solution to the obesity epidemic is the increase in prevalence of childhood obesity (43). This can only lead to the escalating expenditure of health care dollars that will exceed anything we have seen in American medical history thus far (44). In addition, it has been predicted that this current generation of children will be the first in the United States to see a decrease in longevity due to their obesity (45).

Actions speak louder than words, and now is the time to “walk the walk” and not just “talk the talk.” It is our responsibility as health care professionals to do more than just study the obesity epidemic, we need to reverse it. (Other articles in this supplement to the Journal include references 1, 14, and 26.)

I thank Ashley Bourland, Amy Nahigyan, and Mitali Shah for their editorial services provided during manuscript preparation. The author has been a consultant for Novo Nordisk, Arena Pharmaceuticals, Merck Pharmaceuticals, Amylin Pharmaceuticals, GI Dynamics, Johnson & Johnson Inc, Sanofi Aventis Groupe, Orexigen Pharmaceuticals, and Pfizer. She has received research funding from Amylin Pharmaceuticals, Sanofi Aventis Group, Pfizer, Orexigen Therapeutics, MetaProteomics LLC, the Dr Robert C and Veronica Atkins Foundation, Arena Pharmaceuticals, and Gate Pharmaceuticals (a division of Teva Pharmaceuticals USA).
REFERENCES

42. Apovian CM, Kushner R. Does obesity have to be a hormonal disorder for the endocrinologist to take notice? Curr Opin Endocrinol Diabetes Obes. 2004;11:183–5.