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REVİEW ARTICLE

Childhood Obesity: Epidemiological and Clinical Aspects

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Abstract:
Primary childhood obesity has reached epidemic levels in industrialized countries particularly in North America. Twenty five percent of children and adolescents in the United States are overweight and 14% are obese. However, the prevalence of obesity is alarmingly rising in other less developed parts of the world, like Asia, the Middle East and some parts of Africa. Overweight and obesity in childhood extend to adulthood and the majority of obese children grew as obese adults. Obesity has significant impact on both physical and psychological health with serious consequences. The mechanism of development of obesity is not fully understood, and it is believed to be a disorder with multiple causes. Genes are pivotal but, diet and lifestyle preferences, and environmental factors are equally important. There is supporting evidence that excessive intake of sugar-rich soft drink, increased portion size, and steady decline in physical activity have been playing major roles in the current obesity epidemic worldwide. Prevention, not treatment, is the key strategy for controlling childhood obesity. It may be achieved through interventions targeting built environment, physical activity, and diet. This article covers the epidemiologic and clinical aspects of this condition.

Keywords: overweight, fatness, metabolic syndrome, exercise, adiposity
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Introduction

In a small number of cases, childhood obesity is due to pathologic and genetic factors. These include leptin-associated defects, specific genetic syndromes, medical causes such as endocrine disorders, and side effects of medications among others. Obesity not caused by any of these diseases or disorders is often called idiopathic, primary or "simple obesity". The latter name is unfortunate because it may undermine the co-morbidities of obesity and give affected individuals false reassurance about their health. On the other hand, labeling a patient as having idiopathic obesity may waive the need for extensive lab investigations and imaging tests and focuses intervention on prevention and behavior modification. In children obesity, which accompanies certain diseases and pathologic conditions (also called secondary obesity) is usually associated with short stature, while the height is normal and often above average in children who are overweight or have primary obesity. This article addresses epidemiologic and clinical issues, which is pertinent mainly to primary obesity.

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Definition and classification of obesity

The definition of obesity and overweight in humans has changed over time, because of advancement of science and research findings. The word obesity literally refers to a state of excess body fat. Although similar, the term overweight is puristically defined as an excess body weight for height. Because differences in weight among individuals are only partly due to variations in body fat, body weight is a limited, though easily obtainable, index of obesity [1]. Since the adverse consequences of overweight and obesity on health are directly related to excess body fat, the ideal and logical method of classification of obesity should be based on direct measurement of degree of fatness, which is expressed as percentage body fat (PBF), but this may not be easily attainable. There are several methods to measure the total body fat. The research techniques, which are usually precise, include underwater weighing (densitometry), multi-frequency bioelectrical impedance analysis (BIA) and magnetic resonance imaging (MRI). Using these methods, adult males have a PBF of 15-20%, while adult females have a PBF of 25-30% [2]. Although methods such as densitometry are simple and not expensive, they are not practical for clinical settings.

In the clinical environment, techniques such as body mass index (BMI), waist circumference, and waist circumference over hip circumference ratio have been used extensively. Although, these methods are less accurate than the research methods in assessing total body fat, they are satisfactory in identifying the individuals who are at risk of, weight-related, health problems. The BMI, also known as the Quetelet index, is closely correlated with the total amount of body fat, and is used far more commonly than PBF to define obesity [3]. BMI = weight/height^2, where weight is in kilograms and height is in meters. The PBF can be estimated from BMI by using the Deurenberg equation, as follows: PBF = (1.2(BMI) + 0.23) - (10.8{sex} - 5.4), where age is in years and sex is 1 for male and 0 for female. This equation has a standard error of 4% and accounts for approximately 80% of the variation in body fat [4]. Indirect estimation methods for PBF in clinical practice also include the measurement of skin-fold thicknesses (SFT) in one of the four recommended places (i.e., subscapular, triceps, biceps, and suprailiac). Although, there is a high correlation between SFT and PBF as shown in many studies, it can't be used alone as a single marker of obesity.

For large population-based studies and in some clinical situations, BIA is widely used [5]. Cross-sectional studies have shown that BIA predicts total body water (TBW), fat-free mass (FFM), and PBF with high precision [6,7]. Also, it has been shown that BIA provides accurate estimation of changes in PBF and FFM over time [8]. When these techniques are used, the recommended cutoff levels are as follows: For men, PBF greater than 25% defines obesity, and PBF of 21-25% is borderline status. For women, PBF greater than 33% defines obesity, and PBF of 31-33% is borderline status. The cutoff points for excess fatness that defines overweight and obesity in children is slightly different. Williams et al. [9] measured the SFT of 3320 children aged 5–18 years, and used their data to calculate the PBF. They classified children as obese if their PBF were equal or >25% for boys and equal or >30% for girls.

Although, several classifications and definitions for overweight and obesity are available, the most widely accepted is the World Health Organization (WHO) criteria based on BMI. Under this convention for adults, grade 1 overweight (commonly called overweight) is a BMI of 25-29.9 kg/m^2. Grade 2 overweight (commonly called obesity) is a BMI of 30-39.9 kg/m^2. Grade 3 overweight (commonly called morbid obesity) is a BMI equal to or greater than 40 kg/m^2. The surgical literature often uses additional classification to recognize particularly severe forms of obesity. In this setting, a BMI greater than 40 kg/m^2 is described as severe obesity, a BMI of 40-50 kg/m^2 is termed morbid obesity, and a BMI greater than 50 kg/m^2 is termed super obesity. The WHO definition of obesity and overweight in children involves BMIs greater than the 95th percentile for obesity and greater than the 85th percentile for overweight, using the appropriate BMI percentile charts. Same cutoff levels were adopted by the Center for Disease Control and prevention (CDC) in the US [10].

Although, the BMI is typically closely correlated with PBF in a curvilinear fashion, some important caveats to its interpretation apply [11]. In mesomorphic (muscular) persons, BMIs that usually indicate overweight or mild obesity may be spurious, whereas in some persons with sarcopenia or petit

stature, a typically normal BMI may conceal underlying excess adiposity characterized by increased PBF and reduced muscle mass. While BMI seems appropriate for differentiating adults, it may not be as useful in children because of their changing body shape as they progress through normal physical growth. In addition, BMI fails to distinguish between fat and fat-free mass (muscle and bone) and may exaggerate obesity in muscular children. Furthermore, maturation pattern differs between genders and different ethnic groups. The studies that used the BMI to identify overweight and obesity in children and compared the results with the data obtained by the other methods, which are based on percentage of body fat, have found high specificity (95–100%), but low sensitivity (36–66%) for the BMI system of classification [9]. Despite these limitations, BMI remains the only available and practical method for definition of overweight and obesity in children using the WHO criteria.

Apart from total body fat mass, accumulating data suggest that regional fat distribution substantially affects the incidence of co-morbidities associated with obesity. High abdominal fat content (including visceral and, to a lesser extent, subcutaneous abdominal fat) is strongly correlated with worsened metabolic and clinical consequences of obesity [12]. As a result, android obesity, which is predominantly abdominal (apple like), is more predictive of adipose-related co-morbidities than gynecoid obesity (pear like), which has a relatively peripheral (gluteal) distribution. Thus, waist circumference, as a surrogate marker of visceral obesity, has been added to refine the measurement of obesity-related cardiovascular health risks [13].

In adults, waist circumferences greater than 94 cm in men and greater than 80 cm in women and waist-to-hip ratios greater than 0.95 in men and greater than 0.8 in women are the thresholds adopted for significantly increased potential cardiovascular risk [14]. Circumferences of 102 cm in men and 88 cm in women indicate a markedly increased potential risk requiring urgent therapeutic intervention; these are the thresholds used in the definition of the metabolic syndrome [15]. Waist circumference seems to be more appropriate for children because it targets central obesity, which is a risk factor for type 2 diabetes mellitus, hypertension, and coronary heart disease [16]. However, to the best of my knowledge there is no publication on specific cutoff points for waist circumference in children, but there may be some ongoing studies.

Epidemiology

Obesity in children and adults is a worldwide problem, but it reached epidemic levels in the industrialized countries, particularly in North America, in the past decade [17].

The prevalence of childhood obesity in the United States (US) and Canada is increasing alarmingly since 1970 [18]. The problem continues into adult life, because about 70% of obese children and adolescents grow up to become obese adults [19,20]. Currently, twenty-five percent of children in the US are overweight and 14% are obese [21]. Similar pattern is observed in Europe with high prevalence of obesity in the United Kingdom, France, Germany, Spain and Greece and lower rates in Eastern Europe [22-26]. Available data from the WHO multinational project for monitoring trends and determinants of cardiovascular disease (MONICA), suggest that at least 15% of men and 22% of women in Europe are obese [27]. In some European countries such as the Scandinavian countries the prevalence of childhood obesity is lower as compared with countries in the Southern and Mediterranean parts of the continent [28,29]. However, the proportion of obese children is rising in both areas. In Australia, the prevalence of obesity is increasing at an exponential manner, and may reach that of the US in the next decade if the trend continues [30].

Similar data are being reported now from many developing countries, particularly those in Asia and the Middle East. Reports from countries such as Malaysia, Japan, New Zealand, India, and China detail an epidemic of obesity in the past few years [31]. Data from the Middle Eastern countries of Bahrain, Saudi Arabia, Egypt, Jordan, Tunisia, and Lebanon, among others, indicate this same disturbing trend, with alarming levels of obesity often exceeding 40% in adults and particularly worse in women [32-33]. Data from the Caribbean and from South America also highlight similar trends [34]. One study from Saudi Arabia found that one in every six male children, aged 6 to 18 years, is obese and one in four is overweight [35]. In 1998, WHO MONICA group reported Iran as one of the seven countries with the highest prevalence of childhood obesity. This finding

was confirmed by the Isfahan healthy heart study [36]. In both developed and developing countries there are proportionately more overweight and obese girls than boys, particularly among adolescents [37,38]. In adulthood the difference continues and increases with age, and obesity becomes more prominent in women. This gender difference is most likely related to culture, behavior and environmental factors and not to genetic or hormonal effects [39]. In Sub-Saharan Africa, data on childhood obesity are incomplete and scarce. However, a clear and distinct secular trend of profoundly increased prevalence of overweight and obesity is documented by studies in Nigeria and South Africa [40,41].

Although socioeconomic class and the prevalence of childhood obesity are negatively correlated in most of the industrialized countries, this correlation is distinctly reversed in many relatively undeveloped countries, including China, Malaysia, parts of South America, and sub-Saharan Africa. In many of these places obesity and malnutrition coexist, and in some, surprisingly, obesity is becoming more prevalent [42].

Physiological aspects

The adipocyte, which is the cellular basis for obesity, is increasingly found to be a complex and metabolically active cell. At present, the adipocyte is being perceived as an endocrine cell with several peptides and metabolites that may be relevant to the control of body weight [43]. Among the products of the adipocyte involved in complex intermediary metabolic reactions are cytokines, tumor necrosis factor-alpha, interleukin-6, lipotransin, adipocyte lipid-binding protein, acyl-stimulation protein, prostaglandins, adipsin, perilipins, lactate, adiponectin, monobutyrin, and phospholipid transfer protein. The critical enzymes involved in adipocyte metabolism include the endothelial derived lipoprotein lipase (lipid storage), hormone-sensitive lipase (lipid elaboration and release from adipocyte depots), acyl-coenzyme A synthetases (fatty acid synthesis), and a cascade of enzymes that are necessary for beta oxidation and fatty acid metabolism. The ongoing flurry of investigation into the intricacies of adipocyte metabolism in the past few years not only improved our understanding of the pathogenesis of obesity but also offered several potential targets for therapy.

Another area of interest is the investigation of the cues for the differentiation of preadipocytes to adipocytes. With the recognition that this process occurs in white and brown adipose tissue, even in adults, its potential role in the development of obesity and the relapse to obesity after weight loss has become more important than before. Among the identified factors in this process are transcription factors: peroxisome proliferator-activated receptors-gamma (PPAR-gamma); retinoid-X receptor ligands; perilipin; adipocyte differentiation-related protein (ADRP); and CCAAT enhancer-binding proteins [44].

Leptin

Friedman and colleagues discovered leptin (from the Greek word *leptos*, meaning thin) in 1994 and ushered in an explosion of research and a great increase in knowledge about regulation of human feeding and satiation cycle [45]. The leptin receptor is one of the cytokine receptor families of receptors and is activated through the Janus kinases/signal transducers and activators of transcription (JAK/STAT) mechanisms.

Since this discovery, neuromodulation of satiety and hunger with feeding has been found to be far more complex than the old, simplistic model of the ventromedial hypothalamic nucleus and limbic centers of satiety and the feeding centers of the lateral hypothalamus. Leptin is a 16-kD protein produced predominantly in white adipose tissue and, to a lesser extent, in the placenta, skeletal muscle, and stomach fundus in rats. Leptin has a myriad of functions in carbohydrate, bone, and reproductive metabolism that are still being unraveled, but its role in body weight regulation is the main reason it came to prominence [46]. The major role of leptin in body-weight regulation is to signal satiety to the hypothalamus and, thus, reduce dietary intake and fat storage while modulating energy expenditure and carbohydrate metabolism to prevent further weight gain. Unlike the Ob/Ob mouse model in which this peptide was first characterized, most humans who are obese are not leptin deficient but rather leptin resistant. Therefore, they have elevated circulating levels of leptin despite their obesity [47]. Lieb et al assayed plasma leptin in 818 elderly participants in the Framingham Heart Study [48]. Leptin levels, which were higher in women, were strongly correlated with BMI. On

follow-up (mean, 8 y), it was found that congestive heart failure had developed in 129 participants (out of 775 individuals who had been free of congestive heart failure), a first cardiovascular disease event had occurred in 187 participants (out of 532 individuals who had been free of cardiovascular disease), and 391 persons had died. The authors' data, as well as other studies, indicates that higher circulating leptin levels were associated with a greater risk of stroke, ischemic heart disease, and congestive heart failure. However, serum leptin levels did not offer incremental prognostic information beyond BMI or hip/waist ratio [49].

Adiponectin

Obesity is characterized by adipocyte hypertrophy. The adipose tissue serves as the site of triglyceride (TG) storage and free fatty acid/glycerol release in response to changing energy demands. It also participates in the regulation of energy homeostasis as an important endocrine organ that secretes a number of biologically active adipokines such as leptin, adipsin, plasminogen activator inhibitor-1, resistin, and TNF-α . Adiponectin is one such adipokine that has recently attracted much attention.

Adiponectin sensitizes the body to insulin, and acute increment in circulating adiponectin levels triggers a transient decrease in basal glucose levels by inhibiting both the expression of hepatic gluconeogenic enzymes and the rate of endogenous glucose production in experimental animals [50]. In skeletal muscles, adiponectin has been shown to increase expression of molecules involved in fatty-acid transport, in fatty-acid oxidation, and in energy dissipation. These changes led to decreased tissue TG content in skeletal muscle, decrease in plasma glucose and weight loss in mice [51]. Increased tissue TG content has been reported to interfere with insulin-stimulating glucose uptake, leading to insulin resistance. Thus, decreased tissue TG content in muscle improves insulin sensitivity and reduces insulin resistance. Furthermore, it is possible that adiponectin stimulates insulin secretion and regulates energy homeostasis. Adiponectin also increases insulin sensitivity in the liver and alleviate fatty liver diseases and liver fibrosis in mice [52]. Obesity has been reported to be associated with a higher incidence of atherosclerosis and certain cancers. Recently, adiponectin was reported to induce antiangiogenesis and antitumor activity via caspase-mediated endothelial cell apoptosis [53].

Based upon the significant body of evidence shown by them and other researchers, Kadowaki and Yamauchi [54] propose the following adiponectin hypothesis: Reduced adiponectin levels generated by interactions of genetic and environmental factors cause obesity. Reduced adiponectin actions, resulted from down-regulation of adiponectin receptors, are also linked to obesity. These reductions of adiponectin actions may play a crucial causal role in the development of insulin resistance, type 2 diabetes, the metabolic syndrome, and atherosclerosis. According to this adiponectin hypothesis, a therapeutic strategy for type 2 diabetes, obesity, the metabolic syndrome, and cardiovascular diseases may include the up-regulation of plasma adiponectin, up-regulation of adiponectin receptors, or the development of adiponectin receptor agonists.

Socio-cultural perspectives

While obesity is new in human evolutionary history, having been essentially non-existent until about 10 000 years ago, extensive emergence and rise of obesity among most of the world's populations indicates that the ability to become obese is universal [55]. As all aspects of metabolism are under genetic control, and the expression of obesity phenotypes is much more limited than the expression of proteins that regulate metabolism, natural selection for the capacity to save and store energy is likely to have taken place for different genes with the same phenotypic result. It is no surprise, therefore that there are over 600 genes, markers and chromosomal regions identified as being associated with human obesity phenotypes [56]. Environments that allow the expression of these phenotypes have been termed obesogenic. The term 'obesogenic environment' was coined by Swinburn *et al.* who argued that the physical, economic, social and cultural environments of the majority of industrialized nations encourage positive energy balance of their populations [57]. Human exposure to such environments is problematic because, while the energy balance equation is simple (energy intake in excess of expenditure equals weight gain), avoidance of exposure is not. The decline in physical activity in industrialized societies is well documented and as important as food security. Food

security is 'the physical, social and economic access to sufficient, safe and nutritious food that meets the dietary needs and food preferences of a population, for an active and healthy life. Price constrains food choice and purchase among poorer sectors of population, making obesity an issue of food security, and ultimately one of human rights as suggested by Ulijaszek SJ [58]. The positive relationship between socioeconomic status and obesity seen in the past is flattened in developing countries and is inverted in the industrialized societies [59]. The latter has been linked to dietary energy density and energy cost of foods. In recent years, the prices of fresh fruit and vegetables have increased, while those of refined grains, sugars, and fats have declined. Thus energy-dense diets cost less. Class differences in obesity-relevant health behaviors have also been evoked to explain the inverse relationship between socioeconomic status and obesity [60]. Time constraint, particularly in relation to female engagement in the workforce, has seen the emergence and rise in demand for pre-packaged foods, and of food consumption away from the home. The outsourcing of food preparation and demand for convenience in eating has led to decreased number of regular meals and increased snacking in various industrialized nations [61]. Snack foods are often densely caloric, and snacking often takes place without feeling physically hungry, especially when distracted by an external stimulus, such as watching television [62]. It is also more difficult for humans, when they are distracted, to accurately monitor how much they have eaten. Ulijaszek SJ considered obesity a disorder of convenience in modern societies, which is related to human behavior more than human genes [58]. Similar views were expressed by other distinguished researchers [63,64].

Etiology and Pathogenesis

The pathogenesis of obesity is far more complex than the simple paradigm of an imbalance between energy intake and energy output [65,66]. Two major groups of factors with a balance that variably intertwines in the development of obesity are genetics, which is presumed to explain 40-60% of the variance in obesity, and environmental factors [67]. Although the high prevalence of obesity in the children of parents who are obese and the high concordance rate of obesity in identical twins suggest a substantial genetic component to the pathogenesis of obesity, the secular epidemiologic trends of the last few decades suggest an important role for environmental factors. The genetic factors influence the susceptibility of a given child to an obesity-conducive environment. However, the environmental factors such as dietary habits, lifestyle preferences, socio-economic conditions, and cultural behavior seem to play the major role in the rising prevalence of obesity worldwide [68].

Monogenic models for obesity

Although more than 90% of human cases of obesity are polygenic, the recognition of monogenic variants has greatly enhanced our knowledge about the etiopathogenesis of obesity, and provided several potential targets for future anti-obesity medications [69]. Proopiomelanocortin (POMC) and alpha–melanocyte-stimulating hormone (alpha-MSH) both act centrally on the melanocortin receptor 4 (MC 4) to reduce appetite and thus dietary intake [70]. Genetic defects in POMC production and mutations in the *MC4* gene are described as monogenic causes of obesity in humans [71]. Of particular interest is that patients with *POMC* mutations tend to have red hair because of the resultant deficiency in MSH production. Also, because of their diminished levels of adrenocorticotropic hormone (ACTH), they tend to have central adrenal insufficiency. Prohormone convertase is an enzyme that is critical in protein processing, and it appears to be involved in the conversion of POMC to alpha-MSH. The few patients who had been identified to have alterations in this enzyme have clinically significant obesity, hypogonadotropic hypogonadism, and central adrenal insufficiency. This is one of the few models of obesity not associated with insulin resistance. PPAR-gamma is a transcription factor that is involved in adipocyte differentiation. All humans with mutations of the receptor (at band 3p25) described so far have severe obesity. Data suggest that as many as 5% of children who are obese have *MC4* or *POMC* mutations. If confirmed, these would be the most common identifiable genetic defects associated with obesity in humans [72].

The Ob/Ob mice were the prototypical mice that enabled the discovery of leptin. These mice lack the leptin gene and are overweight and hyperphagic with very low levels of serum leptin [73]. A few humans

with a similar genetic defect and similar phenotypic consequences have been identified. This variant of obesity, though minor in the grand scheme of human obesity, is exquisitely sensitive to leptin injection, with reduced dietary intake and profound weight loss. The Db/Db mice have mutations of the leptin receptor in the hypothalamus and the Fa/Fa mice have leptin-receptor mutations in the brain and in peripheral tissues. These mice have early-onset obesity and hyperphagia like the Ob/Ob mice, but they also have normal or elevated serum leptin levels. The human counterparts of this model are rare. Their obesity is associated with hyperphagia, hypogonadotropic hypogonadism, and defective thyrotropin secretion but not associated with hypercortisolism, hyperglycemia, and hypothermia, as occurs in Db/Db mice. In addition to the monogenic models of obesity mentioned above, genome-wide linkage analyses and microarray technology have revealed a rapidly growing list of potential susceptibility obesity genes. Among those identified that are being actively studied are genes on chromosome arms 2p, 10p, 5p, 11q, and 20q [74]. In the same line as the evidence that proved *Helicobacter pylori* as the cause for peptic ulcer disease, evolving data suggest that a notable inflammatory and possibly infective etiology may exist for obesity. Adipose tissue is known to be a repository of various cytokines, especially interleukin-6 and tumor necrosis factor-alpha. Data have shown that adenovirus 36 infection is associated with obesity in chickens and mice. Other data suggest that, though humans who are not obese have a 5% prevalence of adenovirus 36 infection, humans who are obese have a prevalence of 20-30% [75].

Dietary factors

Over the last decades, food has become more affordable to larger numbers of people as the price of food has decreased substantially relative to income and the concept of 'food' has changed from a means of nourishment to a marker of lifestyle and a source of pleasure. Clearly, increases in physical activity are not likely to offset an energy rich, poor nutritive diet. It takes between 1–2 hours of extremely vigorous activity to counteract a single large-sized children's meal at a fast food restaurant, which usually give >785 kcal. The frequent consumption of such a diet can hardly be counteracted by the regular exercise of an average child or adult.

Although overweight and obesity are mostly assumed to be the results of increment in caloric intake mainly in the form of sugars and carbohydrates, without parallel increase in energy expenditure, there is no conclusive evidence for such assumption and results of research are often confusing. Total energy intake expressed as calories is difficult to measure accurately at a population level and even in clinical setting. However, a small caloric imbalance, within the margin of error of estimation methods, is sufficient over a long period of time to lead to overweight and obesity, as reported by previous studies [76]. The methods of identifying frequency of consumption of different food items determine the dietary habits, but estimate caloric intake poorly. Other methods such as 24-hour recall or food diaries evaluate caloric intakes more accurately. However, these methods estimate the short-term pattern, but may fail to predict the long-term intake. With the concurrent rise in prevalence of childhood obesity in the USA, the American National Health and Nutrition Examination Survey (NHANES) noted only subtle change in calorie intake among US children from the 1970s to 1990s. For this period, NHANES found an increased calorie intake only among white and black adolescent females [77]. The same pattern was observed by the latest NHANES (1999–2000). On the other hand, several studies did not find any change of increased energy intake over the years that witnessed the increased prevalence of obesity and overweight. Actually some studies found lower energy intake in recent years compared to the past. The Bogalusa study which has been following the health and nutrition of children since 1973 in Bogalusa (Louisiana, US), reported that total calorie intake of 10-year old children remained unchanged during the period from 1973 to 1988 and a slight but significant decrease was observed when energy intake was expressed per kilogram body weight [78]. The result of a survey carried in five countries in Western Europe suggested that average energy intakes, for all age groups, are lower than they used to be [79]. Some other studies also found similar energy intake among obese children and their lean counterparts [80]. The conclusion from these observations suggests that the amount of consumed calories is not the only determining factor for the development of obesity and other factors are equally important.

Fat intake

For many years, it has been claimed that the increment in the prevalence of pediatric obesity has happened because of an increment in consumption of fatty food, which yields more calories than carbohydrates. Although fat eaten in excess leads to obesity, there is no strong enough evidence that fat intake is the chief reason for the ascending trend of childhood obesity. When evidence was examined, contradictory results have been obtained by cross-sectional and longitudinal studies. The main objection to the notion that dietary fat is responsible for the accelerated pediatric obesity epidemic is the fact that at the same time the prevalence of childhood obesity was increasing, the consumption of dietary fat in different populations was decreasing.

The results of NHANES had shown that fat consumption of American children has fallen over the last three decades [77]. For instance; mean dietary fat consumption in males aged 12–19 years fell from 37.0% (SD = 0.29%) of total caloric intake in 1971–1974 to 32.0% (SD = 0.42%) in 1999–2000. The pattern was the same for females, whose fat consumption fell from 36.7% (SD = 0.27%) of total caloric intake to 32.1% (SD = 0.61%). Gregory et al. [81] reported that the average fat intake of children aged 4–18 years in the United Kingdom is close to the government recommendation of 35% of total energy and it was almost the same over the last thirty years. On the other hand, some cross-sectional studies have reported a positive relationship between fat intake and adiposity in children after controlling for confounding factors [82]. The main source of fat in these studies was the fast food items like hamburgers and hotdog, which contain high concentrations of saturated fat and cholesterol.

Other dietary elements

There is a growing body of evidence suggesting that increasing dairy intake by about two servings per day could reduce the risk of overweight by up to 70% in adults [83]. In addition, calcium intake was associated with 21% reduced risk of development of insulin resistance among overweight younger adults and may reduce risk of development of type 2 diabetes mellitus [84]. On the other hand, there are few studies reporting on the relation between calcium or dairy intake and obesity among children [85]. In these report, higher calcium intake and more dairy servings per day were associated with reduced adiposity in children who were studied longitudinally.

Between 1970 and 1997, the United State Department of Agriculture surveys indicated an increase of 118% of per capita consumption of carbonated drinks, and a decline of 23% for milk and milk-containing drinks [86]. While it is possible that drinking soda instead of milk would result in higher intake of total energy, it cannot be concluded definitively that sugar containing soft drinks promote weight gain because they displace dairy products. However, the boom observed in the soft drink industry and the increased consumption of soft drinks in the past two decades have, undoubtedly, been associated with the epidemic of obesity and type 2 diabetes among children and adults.

Physical Activity

It has been hypothesized that a steady decline in physical activity among all age groups of human population has heavily contributed to rising rates of obesity all around the world. Physical activity strongly influenced weight gain when the confounding effects of energy intake and genetics were controlled for as was shown in a study of monozygotic twins [87]. Numerous studies have shown that sedentary behaviors like watching television and playing computer games are associated with increased prevalence of obesity [88]. In the US, only 25% of adolescents report notable regular physical activity in leisure time, and only 11% of children have regular physical education at school [89]. Several factors, including technology and city environment, contribute to the declining physical activity in the modern life. The availability of electronic household appliances, indoor entertainment tools, lack of safe neighborhood, and lack of public parks discourage physical exercise and outdoor activities [90]. In addition, the low participation rates in sports and physical education in the schools, particularly among adolescent girls and the increased proportions of children who are being driven to school rather than walking are important factors in reducing physical activity, which in turn increased the chances of developing obesity. In addition perception of parents about the weights of their children is often shaded with misjudgment and denial. Furthermore, parents prefer having their children watch television at home rather than play

outside unattended because parents are then able to complete their chores while keeping an eye on their children [91]. Since both parental and children's choices fashion these behaviors, it is not surprising that overweight children tend to have overweight parents and are themselves more likely to grow into overweight adults than normal weight children [92]. In response to the significant impact that the cultural environment of a child has on his or her daily choices of food and activity, promoting a family-centered healthy diet and active lifestyle, through education, motivation, and participation is a promising preventive approach [92].

Consequences of Obesity

Overweight and obesity have significant impact on both physical and psychological health of children. They are associated primarily with metabolic derangement in the form of abnormal glucose tolerance, hyperlipidemia, type 2 diabetes mellitus, and insulin resistance, which constitute the components of the metabolic syndrome [93]. Cardiovascular sequelae in the form of hypertension, ischemic heart disease, pulmonary hypertension, cardiomyopathy, and cardiac failure is noticeable. Pulmonary complications comprise hypoventilation (the Pickwickian syndrome), obstructive sleep apnea, increased predisposition to respiratory infections, and increased incidence of bronchial asthma. GIT complications include reflux esophagitis, steatohepatitis and gall bladder disease. Renal complication presents in the form of proteinuria and focal segmental glomerulosclerosis in severely obese adolescents [94]. Neurological hazards include stroke and idiopathic intracranial hypertension. Moreover, obese individuals are at high risk of suffering from orthopedic, extremities and skin problems [95]. Overweight children followed up for long periods (40 years) were more likely to have cardiovascular, digestive, and respiratory diseases, and die prematurely from any cause as compared with those who were lean [96]. In addition, psychological and behavioral problems such as depression and eating disorders occur with increased frequency in obese children [97].

Prevention

All physicians and researchers agree that prevention is the key strategy for controlling the current epidemic of obesity. Prevention strategies may include primary prevention of obesity in children from infancy through adolescence, by nutritional education or secondary prevention. The latter include prevention of weight regain following weight loss, and avoidance of more weight increment in obese persons unable to lose weight. Until now, most approaches have focused on changing the behavior of adolescents regarding diet and exercise. It seems, however, that these strategies have had little impact on the growing obesity epidemic [98]. While about 50% of the adults are overweight and obese in many countries, it is difficult to reduce excessive weight once it becomes established. Children are therefore the priority population for intervention strategies. Prevention may be achieved through a variety of interventions targeting built environment, physical activity, and diet. These potential strategies can be implemented in preschool, school or after-school institutions as natural settings for influencing the diet and physical activity in children [99]. Implementing similar strategies at home work for both children and parents.

The challenge ahead is to identify all the obesogenic environmental factors and influence them so that healthier choices are more available, easier to access, and widely promoted to a large proportion of the community. The neighborhood is a key setting that can be used for intervention. It encompasses the walking network (footpaths and trails, etc.), the cycling network (roads and cycle paths), public open spaces (parks) and recreation facilities (recreation centers, etc.). While increasing the amount of public open space might be difficult within an existing built environment, protecting the loss of such spaces requires strong support within the community. Although the local environment, both the school and the surrounding community, plays an important role in shaping children's physical activity, the smaller scale of the home environment is also very important in relation to shaping children's eating behaviors and physical activity patterns [100].

Surprisingly, very little is documented about specific home setting influences, and how to use it to make positive changes in diet and exercise habits of the family. Apparently, it is difficult to influence home environment significantly because of the heterogeneity of homes and the limited options for access. Stone and his group had reviewed the impact of 14 school-based interventions on physical activity knowledge and behavior [101]. Most of the outcome

variables showed significant improvements after the intervention. One interdisciplinary intervention program in the US featured a curriculum-based approach to influence eating patterns, reduce sedentary behaviors, and promote higher activity levels among children of school grades six to eight. Evaluation at two years showed a reduction in obesity prevalence in girls (OR = 0.47), but not in boys (OR = 0.85) compared to the control groups. The reduction in television viewing (by approximately 30 min/day) was highly significant for both boys and girls. Significant increment in the percentage of children and adolescents who participate in sports and/or physical education classes at institutions would need policy-based changes at both school and education high administration levels. Similarly, increases in active modes of transport to and from school (walking, cycling, and public transport) would require policy changes at the school and local government levels, as well as support from parents and the community. In some communities a variety of such programs have been implemented e.g. road crossings, 'walking bus', and designated safe walking and cycling routes.

It has been shown that focusing on reducing sedentary behavior and encouraging free play has been more effective than focusing on forced exercise or reducing food intake in preventing already obese children from gaining more weight [102]. Recent efforts in preventing obesity include the initiative of using school report cards to make the parents aware of their children's weight problem. Health report cards are believed to aid prevention of obesity as shown by researchers. In a study in Boston city in the US, parents who received health and fitness report cards were almost twice as likely to know or acknowledge that their children were actually overweight than those parents who did not get a report card [103]. They also were over twice as likely to plan weight-control activities for their overweight children, than non aware parents.

TV watching

Of all aspects of behavior in the home environment, however, television viewing has been researched in greatest detail. Several studies had shown that many children spent >20 h watching TV every week. It appears that gains can be made in obesity prevention through restricting television viewing [104]. Decreasing the time the child spent in front of TV helps in three ways. Firstly, less time of inactivity, secondly reduced eating in front of the television, which is at least as important as increasing activity, and thirdly decreased exposure to food advertisements. Fast foods are one of the most advertised products on television, and children are often the targeted market. Reducing the huge volume of marketing of energy-dense foods and drinks and fast-food restaurants to young children, particularly through the powerful media of television, is a potential strategy that has been advocated. Television advertising to children under the age of 12 years has not been permitted in Sweden since commercial television began over a decade ago. But, children's television programs from other countries, and through satellite television, probably dilute the impact of this ban in Sweden. Norway, Denmark, Austria, Ireland, Australia, and Greece also have some restrictions on television advertising to young children [105]. The fact that children would still be seeing some television advertisements during adult programs or other types of marketing, such as billboards, does not contradict the rationale for the control on the television watching of young children.

Food Sector

Food prices have a marked influence on food-buying behavior and, consequently, on nutrient intake. A small tax (but large enough to affect sales) on high-volume foods of low nutritional value, such as soft drinks, confectionery, and snack foods, may discourage their use. Such taxes are currently applied in some parts of the USA, Canada and some European countries [106]. In addition, food labeling and nutrition 'signposts' such as logos, which indicate that a food meets certain nutrition standards, might help consumers make choices of healthy foods. An example is the 'Pick the Tick' symbol program run by the National Heart Foundations in Australia and New Zealand [107]. The 'Pick the Tick' symbols made it easier for consumers to identify healthier food choices and are frequently used by shoppers. In addition, the nutrition criteria for the products serve as 'de facto' standards for product formulation, and many manufacturers will formulate or reformulate products to meet those standards.

Fat substitutes

One strategy to prevent obesity that is being explored in the dietary industry involves use of fat substitutes [108]. Olestra has been approved for use as a dietary

supplement and additive in various fast foods, such as potato chips and crackers. Olestra has a calorie value of zero kcal/g; whereas fat has approximately 9.1 kcal/g. Olestra consists of a sucrose polyester backbone with 6-8 fatty-acid side chains; this structure making it too large for digestive enzymes of the gut to hydrolyze it. In many trials, olestra had fairly good tolerability, though it apparently is less tasty than materials cooked in regular fat. The major adverse effects reported were flatulence, bloating, diarrhea, and loose stools. Because of the concern for possible malabsorption of fat-soluble vitamins, all olestra-containing foods should be supplemented with these vitamins. Sitostanol is a plant stanol ester preparation that is used as a spread similar to margarine. It blocks cholesterol absorption in the intestine, with no clinically significant alterations in triglyceride or HDL-C values.

Medical Management

Although management of obesity in the individual subject is important, realizing that obesity is a public-health problem is vital. Like all chronic medical conditions, effective management of obesity must be based on a partnership between a highly motivated patient and parents, and a committed team of health professionals. Such team includes physician, psychologist, exercise therapist, dietitian, and other subspecialists, depending on the co-morbidities of the individual patient. The basic principles of management include: (1) eating healthy diet, (2) increasing appropriate physical activity and exercise, (3) reducing time spent in sedentary activities, and (4) modifying behavior. Added to these principles is medication therapy. However, such therapy is still rudimentary in the management of pediatric obesity, and close combination with all the aforementioned modalities is required to achieve substantial and sustained weight loss. At the present time, orlistat is the only medication the US Food and Drug Administration (FDA) has approved for use as an adjunct for weight loss in obese adolescents. Orlistat (Xenical) blocks the action of pancreatic lipase, reducing triglyceride digestion and, thus, absorption [109]. Two major clinical trials showed sustained weight loss of 9-10% over two years. Metformin is approved for use in obese adolescents who have type 2 diabetes mellitus or the full-blown picture of the metabolic syndrome [110]. It decreases the insulin resistance, increases glucose uptake in muscles, decreases hepatic glucose output, and inhibits lipogenesis. A promising future therapy is the newly discovered leptin sensitizers, which may assist in changing feeding habits leading to significant weight reduction [111]. Because children are on growth path, the goal of management of childhood obesity is to reduce the rate of weight gain to fit the profile expected based on normal growth curves. The intent here is not to cause weight loss, which is only needed for adolescents with morbid obesity. Although obesity is associated with increased morbidity and mortality, poorly monitored strict weight loss programs can have equally dire consequences. Among the important potential complications in the setting of weight loss are hypokalemia; cardiac arrhythmias; hypoglycemia; hyperuricemia; and psychologic sequelae, including depression and eating disorders (particularly the binge type).

Available data suggest that a loss of approximately 10% of body weight in subjects who are obese (BMI <40) is associated with virtually maximal benefits regarding obesity-related co-morbidities; therefore, further attempts at weight loss beyond this level are not only unrealistic but also potentially dangerous. This possibility is the basis of a shift in paradigms in the medical management of obesity from a goal of massive weight loss to a goal of maintaining the highest weight possible while still reducing or eliminating obesity-related co-morbidities. On this basis, a reasonable goal for weight-loss in obese adolescents is 0.5-1.0 kg/week. However, the weight-loss goal for each subject must be individualized and based on standard weight-for-height norms [112].

Surgical Care

Surgical therapy is advised only for adolescents with complicated severe obesity. Evidence shows that well-performed bariatric surgery by multidisciplinary team, in carefully selected patients, substantially ameliorates the morbidities associated with severe obesity [113].

Several laparoscopic approaches are available, but the most commonly used are silicone gastric banding; roux-en-Y gastric bypass; liposuction, and horizontal gastroplasty. Although bariatric surgery is the only therapeutic method associated with consistently demonstrable sustained weight loss, it is certainly not

the solution for the growing obesity epidemic. It is expensive, invasive, surgeon specific, and carries risk of anesthetic and procedural complications. The major specific complications associated with surgery are dumping after meals, persistent vomiting, persistent diarrhea, steatorrhea, constipation, hypokalemia, blind-loop syndrome, gallstones, renal stones, metabolic encephalopathy and malabsorption of calcium, folate, iron, thiamine, and vitamin B12. The mortality rate associated with bariatric surgery in standard surgical centers should not exceed 1-2%. The rate is less than 0.5% at centers specializing in bariatric surgery. Despite the morbidity and mortality risk associated with bariatric surgery, the few reports on the follow-up of subjects undergoing these procedures suggest overall improvement in quality of life and body image beside desirable weight loss [114].

Conclusion

Obesity is an escalating global problem, both in children and adults. Treatment options, medical and surgical, are limited and recommended only for small number of patients, who have severe obesity with complications. Therefore, prevention is the cornerstone of intervention. Until recombinant DNA methods are developed enough to enable the alteration of genes that predispose individuals to obesity, the only option available is a massive public health education program with emphasis on healthy food, and active lifestyle. Concerted cooperative approach is needed and should involve public health authorities, schools, families, the fast food industry, and organizers of sports and outdoor games. The results of some public health education initiatives in the US, Singapore and China suggest, that such programs are effective in reducing the prevalence of obesity and its major co-morbidities, such as type 2 diabetes and hypertension. The challenge ahead is to spread and maintain the anti-obesity campaign all over the world. If we fail to do so, obesity will replace tobacco as the leading health hazard in the near future.

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