CHAPTER ONE

1.0 INTRODUCTION

Obesity is a public health problem that has raised concern worldwide. According to the World Health Organization (WHO), there will be about 2.3 billion overweight people aged 15 years and above, and over 700 million obese people worldwide in 2015 [1]. Although a few developed countries such as the United Kingdom and Germany experienced a drop in the prevalence rate of obesity in the past decade, the prevalence of obesity continues to rise in many parts of the world, especially in the Asia Pacific region [2,3]. For example, the combined prevalence of overweight and obesity increased by 46% in Japan from 16.7% in 1976–1980 to 24.0% in 2000, and by 414% in China from 3.7% in 1982 to 19.0% in 2002 [4]. An exhaustive body of literature has emerged to show that overweight and obesity are major causes of co-morbidities, including type II diabetes, cardiovascular diseases, various cancers and other health problems, which can lead to further morbidity and mortality [5,6]. The related health care costs are also substantial. In the United States, the total costs associated with obesity accounted for 1.2% gross domestic product (GDP) [7]. In Europe, up to 10.4 billion Euros was spent on obesity-related healthcare, and the reported relative economic burdens ranged from 0.09% to 0.61% of national GDP [8]. In China, the total medical cost attributable to overweight and obesity was estimated at about 2.74 billion US dollars and these accounted for 3.7% of national total medical costs in 2003 [9]. The total direct costs attributable to overweight and obesity in Canada has been estimated to be 6.0 billion US dollars (of which 66% is attributable to obesity), corresponding to 4.1% of the total health expenditure for 2006. Furthermore, if related co-morbidities were included, the direct cost increased by 25% [10].

1.0.1 DEFINITION OF TERMS

Obesity is a medical condition in which excess body fat has accumulated to the extent that it may have a negative effect on health. People are generally considered obese when their body mass index (BMI), a measurement obtained by dividing a person's weight by the square of the person's height, is over 30 kg/m2, with the range 25–30 kg/m2 defined as overweight. Some East Asian countries use lower values. Obesity increases the likelihood of various diseases and conditions, particularly cardiovascular diseases, type 2 diabetes, obstructive sleep apnea, certain types of cancer, osteoarthritis and depression. Obesity is most commonly caused by a combination of excessive food intake, lack of physical activity, and genetic susceptibility. A few cases are caused primarily by genes, endocrine disorders, medications, or mental disorder. The view that obese people eat little yet gain weight due to a slow metabolism is not generally supported. On average, obese people have a greater energy expenditure than their thin counterparts due to the energy required to maintain an increased body mass.

Obesity is mostly preventable through a combination of social changes and personal choices. Changes to diet and exercising are the main treatments. Diet quality can be improved by reducing the consumption of energy-dense foods, such as those high in fat and sugars, and by increasing the intake of dietary fiber. Medications may be taken, along with a suitable diet, to reduce appetite or decrease fat absorption. If diet, exercise, and medication are not effective, a gastric balloon or surgery may be performed to reduce stomach volume or bowel length, leading to feeling full earlier or a reduced ability to absorb nutrients from food.

Obesity is a leading preventable cause of death worldwide, with increasing rates in adults and children. In 2015, 600 million adults (12%) and 100 million children were obese. Obesity is more common in women than men. Authorities view it as one of the most

serious public health problems of the 21st century. Obesity is stigmatized in much of the modern world (particularly in the Western world), though it was seen as a symbol of wealth and fertility at other times in history and still is in some parts of the world. In 2013, the American Medical Association classified obesity as a disease.

Disease: A disease is a particular abnormal condition, a disorder of a structure or function, that affects part or all of an organism. The study of disease is called pathology which includes the study of cause. Disease is often construed as a medical condition associated with specific symptoms and signs.[1] It may be caused by external factors such as pathogens, or it may be caused by internal dysfunctions particularly of the immune system such as an immunodeficiency, or a hypersensitivity including allergies and autoimmunity. When caused by pathogens (i.e. Plasmodium ssp. in malaria), even in the scientific literature, the term disease is often misleadingly used in the place of its causal agent, viz. the pathogen. This language habitat can cause confusion in the communication of the cause-effect principle in epidemiology, and as such it should be strongly discouraged.

In humans, disease is often used more broadly to refer to any condition that causes pain, dysfunction, distress, social problems, or death to the person afflicted, or similar problems for those in contact with the person. In this broader sense, it sometimes includes injuries, disabilities, disorders, syndromes, infections, isolated symptoms, deviant behaviors, and atypical variations of structure and function, while in other contexts and for other purposes these may be considered distinguishable categories. Diseases can affect people not only physically, but also emotionally, as contracting and living with a disease can alter the affected person's perspective on life.

Death due to disease is called death by natural causes. There are four main types of disease: infectious diseases, deficiency diseases, genetic diseases (both hereditary and

non-hereditary), and physiological diseases. Diseases can also be classified as communicable and non-communicable. The deadliest diseases in humans are coronary artery disease (blood flow obstruction), followed by cerebrovascular disease and lower respiratory infections.

CHAPTER TWO

2.0 EVOLUTIONARY ORIGINS OF OBESITY: A NEW HYPOTHESIS

Obesity is an escalating threat of pandemic proportions, currently affecting billions of people worldwide and exerting a devastating socioeconomic influence in industrialized countries. Despite intensive efforts to curtail obesity, results have proved disappointing. Although it is well recognized that obesity is a result of gene-environment interactions and that predisposition to obesity lies predominantly in our evolutionary past, there is much debate as to the precise nature of how our evolutionary past contributed to obesity. The “thrifty genotype” hypothesis suggests that obesity in industrialized countries is a throwback to our ancestors having undergone positive selection for genes that favored energy storage as a consequence of the cyclical episodes of famine and surplus after the advent of farming 10 000 years ago. Conversely, the “drifty genotype” hypothesis contends that the prevalence of thrifty genes is not a result of positive selection for energy-storage genes but attributable to genetic drift resulting from the removal of predative selection pressures. Both theories, however, assume that selection pressures the ancestors of modern humans living in western societies faced were the same. Moreover, neither theory adequately explains the impact of globalization and changing population demographics on the genetic basis for obesity in developed countries, despite clear evidence for ethnic variation in obesity susceptibility and related metabolic disorders. In this article, we propose that the modern obesity pandemic in

industrialized countries is a result of the differential exposure of the ancestors of modern humans to environmental factors that began when modern humans left Africa around 70 000 years ago and migrated through the globe, reaching the Americas around 20 000 years ago. This article serves to elucidate how an understanding of ethnic differences in genetic susceptibility to obesity and the metabolic syndrome, in the context of historic human population redistribution, could be used in the treatment of obesity in industrialized countries.

Obesity is now a pandemic and is particularly problematic in industrialized countries (1). In the United States and Britain, obesity is rising at a devastatingly rapid rate, and more than half of the population in these countries is now overweight (2, 3). Obesity is a causal factor in numerous metabolic and endocrine disorders including heart disease, diabetes, bone and joint disorders. and some forms of cancer (4–7). Although the social impact and emotional distress obesity can exert are severe, its burden on the economy is crippling. Recent estimates suggest a direct cost in excess of $100 billion per year attributable to the loss of productivity and health care expenditures incurred owing to obesity in the United States (8, 9). It is becoming increasingly clear that whereas detrimental lifestyle changes in recent decades in western societies, particularly of a dietary nature, have contributed to the obesity pandemic, the majority (60%–70%) of individual susceptibility to obesity can be accounted for by genetics (9). The most convincing arguments for this are found twin studies wherein environmental manipulations have been shown to be less important than heritable factors in dictating the degree of weight gain or weight loss.

The explanation for the genetic basis of the current obesity pandemic in industrialized countries is somewhat circumspect, and various theories that attempt to shed light on our understanding of it abound. These theories attempt to reconcile gene-environment interactions with an understanding of human evolution. Two such theories in

particular have gained widespread credibility among geneticists and evolutionary biologists, namely the “thrifty genotype” hypothesis and the “drifty genotype” hypothesis. The thrifty genotype hypothesis argues that the ancestors of present day humans in countries plagued by obesity underwent positive selection for genes that favored “thrift” or energy storage (12). These so-called “thrifty genes” are defined as those that bestow superior energy efficiency such that the energy balance equation is shifted heavily toward energy intake as opposed to energy expenditure (13). The rationale behind this apparent demand for thrifty genes during human evolutionary history is that since the advent of agriculture around 10 000 years ago (13), humanity has been affected by numerous cyclical episodes of “famine” and “feast” whereby periods of food abundance were punctuated by periods of drought. As a result, it is postulated that survival of a population necessitated the selection for thrifty genes that enabled extra fat reserves to be laid down during times of energy surplus to be utilized during harder times. In addition to promoting survival, it is argued that thrifty genes also maintained fertility during periods of famine, a claim that is plausible in light of what is known about the effects of food shortages on reproductive capability (14). The thrifty genotype hypothesis asserts that obesity in industrialized countries is the result of thrifty genes passed down from these ancestors of present day humans who were subject to strong selection pressures that enriched the population with genes that promoted energy storage. Proponents of the theory document various historical famines that occurred on large and devastatingly influential scales in support of it (15). The “drifty phenotype” hypothesis contends that, contrary to being selected for, obesogenic energy-efficient genes favoring fat storage are present in western populations (and all populations worldwide) because early homonids removed the selection pressure that was previously exerted on them by predation (16, 17). The theory, also referred to as the “predation release” theory was put forward by John Speakman to counter the long-held acceptance of the thrifty genotype hypothesis as the most reliable and plausible model for the genetic basis of obesity.

Speakman argued that around 2 million years ago at the dawn of humanity, when the ancient ancestors of modern humans, Homo habilis and Homo erectus, acquired the capability to use fire and stone tools, manufacture weapons, and band together in organized social structures, for the first time in evolutionary history an animal that was not the top predator in its ecosystem was able to remove the threat of predatory danger (16, 17). Thus, as a result, genes imperative for the evasion of predators, such as those that conferred speed, agility, stamina, athletic ability, and leanness (which ensured "survival of the fittest"), were no longer applicable to humans as it was and continues to be for all other animals (18–20). Therefore, the theory suggests that, in the absence of predation selection pressure, genes that promote energy storage and obesity were not removed by natural selection and simply were allowed to drift in the genetic journey of human evolution, such that they explain the obesity pandemic in modern western societies. Although both the thrifty and drifty genotype hypotheses have considerable merit and may be responsible for the genetic susceptibility to obesity, in a portion of individuals, we believe that neither theory can decisively account for the contemporary obesity pandemic in industrialized countries. Advocates of the thrifty hypothesis make the argument that in the postagricultural era (since 10 000 years ago), when humans relinquished their hunter-gatherer lifestyle and put their ability to feed at the mercy of climatic and seasonal events, natural selection enriched the population with thrifty genes that enabled survival during famine (15). However, by 10 000 years ago, modern humans were spread over many areas of the globe, populating Asia, Australasia, Europe, and the Americas and inhabiting a wide range of environments (21–23). Did each of these populations experience the same famine events and agricultural strife? In our view, this is unlikely given that famine with drought, the selection pressure that supposedly drove the evolution of people with thrifty genes, is commonly the result of climate, weather, and disease patterns that are largely governed by local geographical phenomena (24–27). In fact, there is very little evidence of any feast or famine events that would have been

sufficiently consequential to exert their influence over selection for thrifty genes (28, 29). An alternative view of the thrifty gene hypothesis is that positive selection pressure for thrifty genes has been occurring since the evolution of early humans 2 million years ago, preceding the advent of agriculture and before the geographical redistribution and population of modern humans around the globe (15). However, this concept disregards any selection events that might have occurred after modern humans left Africa and populated a diverse range of climates and habitats. The authors of this notion that thrifty genes have been selected for, for longer than the original thrifty hypothesis claimed, state that very few genetic changes have occurred in humans in the last 10 000 years (15). This claim is not, however, borne out by recent evidence. On the contrary, sophisticated and detailed genetic analysis has revealed that a plethora of genetic changes as a result of natural selection in various contemporary human populations have occurred in the last 10 000 to 15 000 years and that these genetic alterations are highly consequential to health and disease in modern times (30). For instance, clear modern selection events in specific geographical populations have greatly enriched genes that confer resistance to malaria (31), enable the ability to digest lactose (32), and protect against kuru (33) and HIV infection (34, 35). Given that immune and digestive functions are intricately linked to metabolism and adiposity (36–39), one cannot dismiss recent selection pressures as being inconsequential to metabolism and the obesity pandemic. Moreover, the global distribution of a large amount of single nucleotide polymorphisms in contemporary human populations has been shown to have a strong latitudinal basis, suggesting a clear climatic and geographical selection influence (40). These observations underscore not only that recent selection events have shaped the genetics of present day humans but also that genetic influences on health and disease, including obesity, must factor in ethnic and geographical considerations. Thus, in our view, the thrifty hypothesis is not an accurate reflection of historical positive selection events. In a similar fashion, the drifty genotype hypothesis assumes that since 2 million years ago the ancestors of modern humans have

been subject to the same evolutionary events (ie, release from predation) that have subsequently endowed present day humans in industrialized countries with thrifty genes due to genetic drift. However, this theory makes no attempt to consider the impact on obesity of distinct selection events, specific to geographical influences that may have shaped human evolution since modern humans left Africa 60 000 years ago. It is becoming increasingly clear that genetic susceptibility to obesity is not equal across the various ethnic groups whose ancestors experienced vastly different geographical and environmental selection pressures (41–44). We believe that to understand the modern obesity phenomenon in industrialized countries, changing population demographics with regard to ethnic variation must be taken into account. Although the ethnic variation in obesity susceptibility has been reviewed extensively and accurately in recent years (45–51), none of this research has served to understand the cause of the variability in obesity susceptibility between ethnicities or how evolutionary forces relating to climate may have shaped the current obesity pandemic. We believe that by understanding the ethnic basis for obesity susceptibility in the light of evolutionary events, western societies will be a step closer to deciphering the mysteries surrounding the genetic predisposition or resistance to obesity.

Although it is our belief that genetic influences are predominantly responsible for explaining the ethnic variation in obesity, it is nonetheless important to recognize that obesity is a complex, multifactorial problem, and therefore other nongenetic factors almost certainly play a role in its pathogenesis. To this end, socioeconomic factors, including education, income, and health care, which have been shown to be ethnically biased, are strongly correlated with obesity trends. Therefore, although the focus of the present article is entirely on the genetic basis for the ethnic variation in obesity, we stress that it does not make an exclusive claim on the origins of obesity.

2.0.1 CLASIFFICATION OF OBESITY

Obesity is a medical condition in which excess body fat has accumulated to the extent that it may have an adverse effect on health.[19] It is defined by body mass index (BMI) and further evaluated in terms of fat distribution via the waist–hip ratio and total cardiovascular risk factors.[20][21] BMI is closely related to both percentage body fat and total body fat.[22] In children, a healthy weight varies with age and sex. Obesity in children and adolescents is defined not as an absolute number but in relation to a historical normal group, such that obesity is a BMI greater than the 95th percentile.[23] The reference data on which these percentiles were based date from 1963 to 1994, and thus have not been affected by the recent increases in weight.[24] BMI is defined as the subject's weight divided by the square of their height and is calculated as follows.

$$\mathrm{BMI} = \frac{m}{h^2}$$

where m and h are the subject's weight and height respectively.

BMI is usually expressed in kilograms per square metre, resulting when weight is measured in kilograms and height in metres. To convert from pounds per square inch multiply by 703 (kg/m2)/(lb/sq in).[25]

The most commonly used definitions, established by the World Health Organization (WHO) in 1997 and published in 2000, provide the values listed in the table.[26][27]

Some modifications to the WHO definitions have been made by particular organizations.[28] The surgical literature breaks down class II and III obesity into further categories whose exact values are still disputed.[29]

Any BMI ≥ 35 or 40 kg/m2 is severe obesity.

A BMI of ≥ 35 kg/m2 and experiencing obesity-related health conditions or ≥40–44.9 kg/m2 is morbid obesity.

A BMI of ≥ 45 or 50 kg/m2 is super obesity.

As Asian populations develop negative health consequences at a lower BMI than Caucasians, some nations have redefined obesity; Japan have defined obesity as any BMI greater than 25 kg/m2[8] while China uses a BMI of greater than 28 kg/m2.[28]

CHAPTER THREE

3.0 CAUSES OF OBESITY

At an individual level, a combination of excessive food energy intake and a lack of physical activity is thought to explain most cases of obesity.[81] A limited number of cases are due primarily to genetics, medical reasons, or psychiatric illness.[9] In contrast, increasing rates of obesity at a societal level are felt to be due to an easily accessible and palatable diet,[82] increased reliance on cars, and mechanized manufacturing.[83][84] A 2006 review identified ten other possible contributors to the recent increase of obesity: (1) insufficient sleep, (2) endocrine disruptors (environmental pollutants that interfere with lipid metabolism), (3) decreased variability in ambient temperature, (4) decreased rates of smoking, because smoking suppresses appetite, (5) increased use of medications that can cause weight gain (e.g., atypical antipsychotics), (6) proportional increases in ethnic and age groups that tend to be heavier, (7) pregnancy at a later age (which may cause susceptibility to obesity in children), (8) epigenetic risk factors passed on generationally, (9) natural selection for higher BMI, and (10) assortative mating leading to increased concentration of obesity risk factors (this would increase the number of obese people by increasing population variance in weight).[85] While there is substantial evidence supporting the influence of these mechanisms on the increased prevalence of obesity, the evidence is still inconclusive, and the authors state that these are probably

less influential than the ones discussed in the previous paragraph.

Diet

A 2016 review supported excess food as the primary factor.[87] Dietary energy supply per capita varies markedly between different regions and countries. It has also changed significantly over time.[86] From the early 1970s to the late 1990s the average food energy available per person per day (the amount of food bought) increased in all parts of the world except Eastern Europe. The United States had the highest availability with 3,654 calories (15,290 kJ) per person in 1996.[86] This increased further in 2003 to 3,754 calories (15,710 kJ).[86] During the late 1990s Europeans had 3,394 calories (14,200 kJ) per person, in the developing areas of Asia there were 2,648 calories (11,080 kJ) per person, and in sub-Saharan Africa people had 2,176 calories (9,100 kJ) per person.[86][88] Total food energy consumption has been found to be related to obesity.[89] The widespread availability of nutritional guidelines[90] has done little to address the problems of overeating and poor dietary choice.[91] From 1971 to 2000, obesity rates in the United States increased from 14.5% to 30.9%.[92] During the same period, an increase occurred in the average amount of food energy consumed. For women, the average increase was 335 calories (1,400 kJ) per day (1,542 calories (6,450 kJ) in 1971 and 1,877 calories (7,850 kJ) in 2004), while for men the average increase was 168 calories (700 kJ) per day (2,450 calories (10,300 kJ) in 1971 and 2,618 calories (10,950 kJ) in 2004). Most of this extra food energy came from an increase in carbohydrate consumption rather than fat consumption.[93] The primary sources of these extra carbohydrates are sweetened beverages, which now account for almost 25 percent of daily food energy in young adults in America,[94] and potato chips.[95] Consumption of sweetened drinks such as soft drinks, fruit drinks, iced tea, and energy and vitamin water drinks is believed to be contributing to the rising rates of obesity[96][97] and to an increased risk of metabolic syndrome and type 2 diabetes.[98] Vitamin D deficiency is

related to diseases associated with obesity.[99] As societies become increasingly reliant on energy-dense, big-portions, and fast-food meals, the association between fast-food consumption and obesity becomes more concerning.[100] In the United States consumption of fast-food meals tripled and food energy intake from these meals quadrupled between 1977 and 1995.[101]

Sedentary lifestyle

A sedentary lifestyle plays a significant role in obesity.[105] Worldwide there has been a large shift towards less physically demanding work,[106][107][108] and currently at least 30% of the world's population gets insufficient exercise.[107] This is primarily due to increasing use of mechanized transportation and a greater prevalence of labor-saving technology in the home.[106][107][108] In children, there appear to be declines in levels of physical activity due to less walking and physical education.[109] World trends in active leisure time physical activity are less clear. The World Health Organization indicates people worldwide are taking up less active recreational pursuits, while a study from Finland[110] found an increase and a study from the United States found leisure-time physical activity has not changed significantly.[111] A 2011 review of physical activity in children found that it may not be a significant contributor.[112]

In both children and adults, there is an association between television viewing time and the risk of obesity.[113][114][115] A review found 63 of 73 studies (86%) showed an increased rate of childhood obesity with increased media exposure, with rates increasing proportionally to time spent watching television.[116]

Genetics

A painting of a dark haired pink cheeked obese nude young female leaning against a table. She is holding grapes and grape leaves in her left hand which cover her genitalia.

A 1680 painting by Juan Carreno de Miranda of a girl presumed to have Prader–Willi syndrome[117] Like many other medical conditions, obesity is the result of an interplay between genetic and environmental factors.[118] Polymorphisms in various genes controlling appetite and metabolism predispose to obesity when sufficient food energy is present. As of 2006, more than 41 of these sites on the human genome have been linked to the development of obesity when a favorable environment is present.[119] People with two copies of the FTO gene (fat mass and obesity associated gene) have been found on average to weigh 3–4 kg more and have a 1.67-fold greater risk of obesity compared with those without the risk allele.[120] The differences in BMI between people that are due to genetics varies depending on the population examined from 6% to 85%.[121] Obesity is a major feature in several syndromes, such as Prader–Willi syndrome, Bardet–Biedl syndrome, Cohen syndrome, and MOMO syndrome. (The term "non-syndromic obesity" is sometimes used to exclude these conditions.)[122] In people with early-onset severe obesity (defined by an onset before 10 years of age and body mass index over three standard deviations above normal), 7% harbor a single point DNA mutation.[123] Studies that have focused on inheritance patterns rather than on specific genes have found that 80% of the offspring of two obese parents were also obese, in contrast to less than 10% of the offspring of two parents who were of normal weight.[124] Different people exposed to the same environment have different risks of obesity due to their underlying genetics.[125]

Other illnesses

Certain physical and mental illnesses and the pharmaceutical substances used to treat them can increase risk of obesity. Medical illnesses that increase obesity risk include several rare genetic syndromes (listed above) as well as some congenital or acquired conditions: hypothyroidism, Cushing's syndrome, growth hormone deficiency,[129] and the eating disorders: binge eating disorder and night eating syndrome.[2] However,

obesity is not regarded as a psychiatric disorder, and therefore is not listed in the DSM-IVR as a psychiatric illness.[130] The risk of overweight and obesity is higher in patients with psychiatric disorders than in persons without psychiatric disorders.[131]

Certain medications may cause weight gain or changes in body composition; these include insulin, sulfonylureas, thiazolidinediones, atypical antipsychotics, antidepressants, steroids, certain anticonvulsants (phenytoin and valproate), pizotifen, and some forms of hormonal contraception.[2]

Social determinants

The disease scroll (Yamai no soshi, late 12th century) depicts a woman moneylender with obesity, considered a disease of the rich. While genetic influences are important to understanding obesity, they cannot explain the current dramatic increase seen within specific countries or globally.[132] Though it is accepted that energy consumption in excess of energy expenditure leads to obesity on an individual basis, the cause of the shifts in these two factors on the societal scale is much debated. There are a number of theories as to the cause but most believe it is a combination of various factors.

The correlation between social class and BMI varies globally. A review in 1989 found that in developed countries women of a high social class were less likely to be obese. No significant differences were seen among men of different social classes. In the developing world, women, men, and children from high social classes had greater rates of obesity.[133] An update of this review carried out in 2007 found the same relationships, but they were weaker. The decrease in strength of correlation was felt to be due to the effects of globalization.[134] Among developed countries, levels of adult obesity, and percentage of teenage children who are overweight, are correlated with income inequality. A similar relationship is seen among US states: more adults, even in higher social classes, are obese in more unequal states.[135] Many explanations have been put

forth for associations between BMI and social class. It is thought that in developed countries, the wealthy are able to afford more nutritious food, they are under greater social pressure to remain slim, and have more opportunities along with greater expectations for physical fitness. In undeveloped countries the ability to afford food, high energy expenditure with physical labor, and cultural values favoring a larger body size are believed to contribute to the observed patterns.[134] Attitudes toward body weight held by people in one's life may also play a role in obesity. A correlation in BMI changes over time has been found among friends, siblings, and spouses.[136] Stress and perceived low social status appear to increase risk of obesity.[135][137][138] Smoking has a significant effect on an individual's weight. Those who quit smoking gain an average of 4.4 kilograms (9.7 lb) for men and 5.0 kilograms (11.0 lb) for women over ten years.[139] However, changing rates of smoking have had little effect on the overall rates of obesity.[140]

In the United States the number of children a person has is related to their risk of obesity. A woman's risk increases by 7% per child, while a man's risk increases by 4% per child.[141] This could be partly explained by the fact that having dependent children decreases physical activity in Western parents.[142]

Gut bacteria

The study of the effect of infectious agents on metabolism is still in its early stages. Gut flora has been shown to differ between lean and obese humans. There is an indication that gut flora in obese and lean individuals can affect the metabolic potential. This apparent alteration of the metabolic potential is believed to confer a greater capacity to harvest energy contributing to obesity. Whether these differences are the direct cause or the result of obesity has yet to be determined unequivocally.[146] An association

between viruses and obesity has been found in humans and several different animal species. The amount that these associations may have contributed to the rising rate of obesity is yet to be determined.[147]

3.0.1 PREVENTIVE MEASURES OF OBESITY

The prevention of obesity is a topic that must be considered given the major increases both in the prevalence of obesity and in the mean body weights of people in the United States over the past decade .Despite the appeal of prevention as an ideal, it appears that this country as a whole has been unable to prevent obesity. The results of more limited and focused efforts at prevention, described later in this chapter, have hardly been more successful. These facts led a recent review to conclude that "we have not been able to prevent obesity in the past and we do not have the tools to do better in the future" (Stunkard, in press).

It has been proposed that genetic vulnerability may lie at the root of the current epidemic of obesity and the problem of controlling, let alone preventing, obesity (Bouchard, 1994). However, there has been no real change in the gene pool during this period of increasing obesity. The root of the problem, rather, must lie in the powerful social and cultural forces that promote an energy-rich diet and a sedentary lifestyle. But if social and cultural forces can promote obesity, these same forces should be able to control it. Therein lies the still unrealized potential for preventing obesity. There is some ambiguity of terminology in the prevention literature. The verb prevent implies taking an action or interposing an impediment to stop or keep something from happening. Different ideas about what it is that should be stopped or kept from happening have been suggested in terms of obesity prevention. Is it the incidence of obesity itself? Is it preventing weight gain among those treated for obesity to prevent progression from a moderate to more severe levels? Does the success of prevention efforts depend upon the effect on comorbid

medical disabilities (e.g., diabetes or hypertension)? Is what should be stopped or kept from happening an underlying risk condition or predisposition factor for obesity development? A recent Institute of Medicine (IOM) report recommends an approach to clarifying definitions of prevention that, although developed in relation to mental disorders, apply to obesity (IOM, 1994). This IOM report reviews existing classification systems for preventive interventions for physical illness. The familiar public health classification system designates three types of prevention: primary, secondary, and tertiary. The goal of primary prevention is to decrease the number of new cases (incidence) of a disorder. In secondary prevention, the goal is to lower the rate of established cases of the disorder in the population (prevalence). Tertiary prevention seeks to stabilize or decrease the amount of disability associated with an existing disorder. For obesity, tertiary prevention could refer to decreasing the progression to more severe obesity or decreasing the likelihood of associated musculoskeletal, metabolic, or vascular disorders (e.g., osteoarthritis, diabetes, or cardiovascular disease).

When this prevention classification system was introduced more than 25 years ago, the implicit disease model was one of an acute condition with a specific and unifactorial cause. It was assumed that mechanisms linking the cause of a specific disease to its subsequent occurrence could be identified. In the intervening years, many chronic diseases prevalent in this country have been recognized as having multifactorial etiologies. Research on these diseases has advanced our knowledge about the complicated relations that exist between risk factors and protective factors for disease and the outcomes of preventive interventions. But this knowledge can breed the pessimistic view that prevention efforts will be futile until the etiologies of diseases are better understood (IOM, 1994).

According to this analysis, the concept of risk reduction is critical to prevention programs and research. Addressing the degrees of risk for a condition supplants the more

simplistic concept of prevention in which a disease is simply present or absent. Risk factors refer to those characteristics that, if present for a particular individual, make it more likely that this person (compared to someone selected from the general population) will develop a disorder (Werner and Smith, 1992). Both risk and protective factors are included here. Research also shows that many at-risk individuals have factors in their background or environment that protect against the development of a disorder (Garmezy, 1983).

At the current stage of research into preventing obesity, work is still in the first two phases of this research cycle: identifying high-risk and protective factors for the development of obesity, and determining which factors are malleable and can be altered by preventive interventions. We recommend continuing this early research on the determinants of obesity and pilot-testing promising interventions before funds are allocated for large-scale community prevention trials.

The recent IOM report also recommended an alternative terminology for physical disease prevention, proposed by Gordon (1987), and we adopt it here (see Figure 9-1). This terminology identifies three types of prevention: universal, selective, and indicated prevention. Each category represents a population group, rather than a disorder or disease state, to whom preventive interventions are directed. Universal preventive measures or interventions are designed for everyone in the eligible population. Selective preventive measures are directed toward a subgroup of the population whose risk of developing the disorder is above average or high. Indicated preventive interventions are targeted to high-risk individuals identified as having minimal but detectable signs or symptoms that foreshadow the disorder, or exhibiting biological markers indicating predisposition, who do not meet the full diagnostic criteria for the disorder itself.

The earlier IOM report reserves the term prevention for those interventions that occur

before the onset of a diagnosed disorder. What was previously known as tertiary prevention is redefined as maintenance intervention , whose aim is to reduce the disability associated with an ongoing disorder. Maintenance interventions, which can be supportive, educational, and/or pharmacological, are provided on a long-term basis to reduce relapse and recurrence. Consistent with the IOM definition of prevention (i.e., interventions that occur before onset),

The primary aim of obesity prevention is to reduce the number of new cases of obesity. This can be accomplished by means of a risk-reduction model. Even if the obesity outcomes are in the distant future, the decrease in risk factors and increase in protective factors for obesity can be identified. An important secondary aim is to delay the onset of obesity. The goals of indicated prevention programs are harder to define than those of universal and selective prevention programs. They might be framed in terms of reducing the length of time initial weight gain persists beyond certain pre-obese limits and halting its progression before diagnostic criteria for obesity are met. Even if the individual does eventually develop obesity, the prior preventive intervention may still have had an effect by reducing the duration or severity of the disorder.

CHAPTER FOUR

4.0 RECOMMENDATION AND CONCLUSION

We believe that a fundamental failure to understand the genetic basis for the ethnic variability in susceptibility to obesity in the developed world is a contributory factor in the modern obesity pandemic in these countries. The obesity pandemic has coincided with not only an increase in poor eating habits but also mass immigration of various ethnicities in these countries. Whereas the thrifty and drifty genotype hypotheses make the assumption that the selection pressures faced by the ancestors of all inhabitants of developed countries today were the same, we have argued that this is not entirely

accurate. The descendants of early humans who remained in Africa and those who migrated to equally tropical or subtropical environments such as black Americans and Pacific Islanders maintained heat adaption genes. The descendants of those who migrated to colder regions such as Europe and Siberia such as Caucasians and Chinese acquired genes for cold adaptation. A group of early Siberians who migrated to the Americas and settled in subtropical regions in North and Central America lost their cold adaptive genes and reacquired genes for heat adaptation. We postulate that positive selection for cold adaptation in their ancestors equips Caucasians and East Asians such as Chinese, Japanese, and Koreans with efficient BAT and UCP1 function, an advantageous by-product of which is a higher metabolic rate and resistance to obesity. The opposite is true for Africans and South Asians whose ancestors had no need to evolve efficient BAT and UCP1 function, resulting in an increased propensity for obesity in these populations when combined with a sedentary and hypercaloric western lifestyle. Figure 1 is a diagrammatic representation of the impact of historical human migration on selection of genes for heat and cold adaptation and consequent obesity prevalence in industrialized countries today. In summary, we suggest that the modern obesity pandemic in the developed world is largely due to differential climatic exposure of the ancestors of present day people in these countries as a result of historical human migration that began when modern humans left Africa 40 000 to 60 000 years ago. This new perspective has crucial implications for combating obesity in industrialized countries.

Many approaches to prevent obesity appear promising, though few studies are available to document long-term positive outcomes. Since success in prevention programs is often equated with the absence of future problems, the impact of universal prevention programs that target education and behavior change (e.g., in diet or exercise patterns) is difficult to evaluate except through longitudinal population studies. The recent literature in prevention has focused more on working with groups or individuals

who are known to be at risk for a particular disorder. The emphasis on working with high-risk individuals with interventions that are matched or targeted to specific risk factors (as in selective and indicated prevention strategies) appears to have considerable merit. Only a few studies of this type have been conducted in obesity prevention. Future research on the development of prevention programs targeted to those at high risk for obesity is necessary before any conclusions can be drawn concerning this promising new approach.

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