Changing Perspective on Obesity: Genetic and Environmental Health Consequences in the Offspring

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Abstract

The prevalence of obesity and overweight has reached epidemic proportions with globally more than 1 billion adults being overweight and an estimated 400 million clinically obese with a projected rise to over 700 million by 2015[1]. The condition – once affecting only high-income countries – is now a major global health concern touching all communities across all ages and socioeconomic groups. The traditional view that overweight and obesity is exclusively the result of over-indulgence in energy-dense, nutrient-poor foods with high levels of sugar and saturated fats is widespread. This is not necessarily the case promoting an urgent need to raise awareness about the multidisciplinary origins of this condition. For example; maternal exposure to a variety of fat-dense diets under differing environmental conditions and fetal developmental phases may adversely impact upon metabolic parameters predisposing the infant to an increased risk of overweight and obesity in early childhood, and reduced fertility later in adult life. By emphasizing that the condition maybe the product of both past and present circumstance, we are challenging contemporary food security improvements. It is for this reason that the present review focuses on both the science and the ethics. Bioscience ethics can usefully be linked to the discipline of epigenetics – namely environmentally triggered changes in gene expression promoting lasting legacies in subsequent generations. Importantly, epigenetic insights reveal how positive or negative environmental influences may promote resilience, or otherwise, in the offspring. By integrating ethics and the life sciences, unique educational opportunities for advancing biological understanding within the scaffolding of ethics can be created.

Keywords: Obesity, fetal metabolic programming, epigenetics/epigenome, bioscience ethics, addiction, stress.

Introductory Background

Obesity, the prevalence of which has seen an almost exponential rise, is an “energy imbalance” disorder resulting in excess fat accumulation in the body, mostly within the subcutaneous tissues. The accumulation of fat, stored mostly as triglycerides in adipose tissue, is caused by a greater caloric ingestion than is required for producing energy needed in daily activities. The most widely used measure to indicate the presence of this condition is body mass index (BMI), which, by comparative analysis of an individual’s weight to height ratio, determines a range of adaptive body fat percentages. A BMI of 25-30kg/m² is defined as a state of overweight, whereas a state of clinical obesity is represented by a BMI of greater than 30kg/m²[1]. When body mass indices are referred to in this review, obesity is defined as a body mass index of ≥30kg/m². It is important that attention be drawn to the fact that this body index does not take into account individual body characteristics such as differing body type morphologies, athletic versus shapely, nor does it allow for measurements of weight to specify bone and muscle density. By considering only total individual mass and excluding metabolic efficiency, obesity simply highlights a condition of over-consumption. While it is undeniable that obesity is a result of energy intake and expenditure imbalance, underlying aetiologies may suggest, for example, alteration in glucose and lipid metabolism[2] or vascular dysfunction[3].

An appetite for foods dense in fats and sugars is the result of selection of adaptive physiological characteristics that evolved in our distant hunter-gatherer ancestors. During that phase of our evolution the ability to store energy reserves in the form of adipose tissue was adaptive in seasonal environments where periods of limited food availability – starvation even – was predictable[4,5]. Since then our physiology has remained little unchanged; thus, in contemporary society where foods are abundant, individuals are ill adapted to this newfound bounty currently triggering a global epidemic of morbidity and ill health[6,7,8].

Obesity in Pregnancy and Early Infancy: Long-Term Metabolic Consequences

There exist periods of vulnerability during fetal development where the types of foods the mother eats may increase the risk of overweight and obesity in the offspring. For example, during the third trimester of pregnancy, epigenetic drivers in the form of increased portions of processed, energy-dense maternal food intake, will up-regulate the transport of lipids as free fatty acids across the placenta which, in turn, will accelerate the generation of fat cells within fetal adipose tissue[9,10]. Development of additional fat cells, in unison with increased fetal/placental circulating levels of leptin, is likely to predispose the offspring to a larger than average gestational weight and increased appetite during childhood; thus, perpetuating the trans-generational effects of overweight and obesity[11]. Leptin, the hormonal product of the OB (obesity) gene, is produced in adipose tissue and plays a significant role in the central regulation of energy expenditure (including appetite and metabolism) as monitored by the ‘appetite centre’ of the brain’s hypothalamus[4,12]. Under normal adult conditions, leptin acts as an endocrine signal on the hypothalamic receptors

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where it inhibits appetite; however, consistently elevated leptin levels, as in obesity, may impair this function. On the other hand, leptin – also widespread in fetal and placental tissues – acts as a potent fetal growth factor [9]. Before birth, leptin production promotes growth by increasing the mobilization of maternal fat stores in order to further support fetal growth. It should be noted that towards term, a number of structural and functional maturational changes occur in the fetus in preparation for the transition from intrauterine to extrauterine life. Particularly relevant to the present discussion is that during the last trimester’s growth phase, fat represents over 50% of fetal caloric accretion.

Maternal ‘flavour preference’ can also be passed on to the offspring during the period of breastfeeding, as well as during third trimester gestation. Clinical trials monitoring possible periods of flavour development preferences identified a critical period spanning 3-4 months postnatally [13]. Infants were exposed to two baby formulae with differing flavour characteristics; cow’s milk-based and hydrolysed protein-based milk. Despite a sour, bitter taste and unpleasant odour, infants that were previously exposed to the hydrolysed protein-based formula over the four month course of the trial, became more accepting of the unpalatable formula [13]. Similarly, exposure to specific nutrient-dense foods during breastfeeding can result in infant preference to this specific food type. For example, earlier clinical trials found that the type of formula fed during infancy influenced taste preference at ages 4-5 years [14].

These and similar findings demonstrate that early exposure to specific ‘flavours’ does impact upon learned food preference where behavioural association with energy-dense foods established during critical developmental periods, may affect certain neurological adaptations that increases a distinctive pleasant reinforcement response, when the food is consumed later in life. As a consequence, the beginnings of overweight and obesity are partly contributed to by intrauterine conditions during development, as well as infancy and dietary choices made in later life. For this reason, it is crucial that informed parental behaviours associated with food intake are established prior to gamete formation and conception, as well as during pregnancy and breastfeeding. Parents, who are better informed about reproductive physiology [15], become more responsible behaviourally, reducing the risk of their offspring developing obesity or overweight [16]. Awareness of how individual choice and circumstance can influence both individual and generational health, through the advancement of biological knowledge of both the genetic and epigenetic contributors to a high body mass index, will improve societal and individual understanding of obesity.

**Obesity and Fertility Outcome**

Individuals who are more vulnerable to a genetic predisposition of higher body weight often experience reduced reproductive fitness. A greater weight, especially distributed around the abdominal region, is associated with reduced fertility in both women and men. Fertility irregularities can be identified early via changes to the balance of circulating hormones; such as leptin, which can result in adverse effects controlling normal regulation of neuroendocrine function driving maturational changes towards the attainment of puberty [17]. As described above, leptin (part of the adipokine regulating system) is a product of adipose tissue so circulates in the body at a higher concentration in obese or overweight persons, compared to those of lesser mass. The adipokine system is central in the adjustment and timing of the onset of gonadotropin-releasing hormone (GnRH) secretion that drives the hypothalamic-pituitary-gonadal axis to initiate the processes that culminate in puberty [18]. Owing to high circulating levels of leptin in overweight young girls, the onset of puberty is premature compared to their lesser weight associates. With the occurrence of the first menses at an earlier age, it is also predicted that this group of women will experience menopause at an earlier age [19,20]. In any event, it has been well established that a state of obesity influences fertility in reproducitively active women by adversely affecting the development of gametes (eggs) that may then contribute to the trans-generational effect of obesity and possible reduced fertility in turn [21]. Decreased reproductive capability, or fitness of offspring, is further enhanced when the gamete is fertilized by a male partner who is also overweight or obese.

Male infertility has been little discussed until recently with the primary focus for its cause attributed to an imbalance of hormone concentrations. As a greater weight reduces metabolism essential for sperm serum production, men who are overweight or obese often have decreased plasma levels of sex hormone-binding globulin (SHBG), which lowers the level of circulating steroid hormones [22, 23]. Men with a body mass index exceeding 30kg/m², with a large proportion of adipose tissue distributed around the abdominal region, are further likely to experience lower levels of total testosterone and free testosterone due to the enzyme aromatase in fat tissue, which aromatizes testosterone to estrogen [24]. The combination of reduced semen quality and low testosterone, progressively result in lower sperm count, increased sperm with abnormal morphology and decreased fertilizability [25]. Overweight or obese individuals are approximately three times more likely to develop these fertility anomalies than men with a body mass index of less than 30kg/m² [26]. As a result, clinically obese men are more likely to have greater fertility difficulties that may adversely affect the next generation of infants: hence, further contributing to the trans-generational effects of obesity.

As many individuals are unaware of the progressive generational predisposition to inherit reduced fertility status, it is crucial that information regarding the influence of obesity and overweight on future generations be made available. By distributing knowledge of the applied science through bioethics
education, individuals can be made more aware of their choices and provide better long-term health in offspring by reducing their vulnerability to develop the basis of adult disease in utero.

**Sedentary Lifestyle and Increased Food Availability**

Since the beginnings of human evolution, we have adapted physiological mechanisms to cope with daily requirements of physical exertion and the storage of energy reserves for periods of starvation. Progressively leading into the 21st century, lifestyles have adapted to become more sedentary with a lessened physical role in both the workforce and traditional home functions. As technological advances have allowed us to become more efficient in daily processes, the energy requirement for daily function is much lower now than a century ago. Hypothetical models of energy requirement have estimated total daily expenditure a century ago to be around 3000 kcal/day whilst under modern living conditions, daily energy requirement for physical activity is estimated around 500-1000 kcal/day; 30-60% lower than past decades [27]. In addition, total body fat composition is negatively correlated with basal metabolic rate (BMR) because fat consumes lower energy per unit weight compared with muscle [28]. For this reason, individuals with an inherited predisposition to store excess fat may, involuntarily, be more likely to gain weight as a result of a sedentary lifestyle. Further, as a result of physiological adaptation to a higher daily caloric intake and levels of circulating dopamine – the feel good neuro-hormone – individuals can develop an addiction to our primordial taste preference, increasing the risk of developing overweight or clinical obesity. However, despite the nature of the workforce changing, there still remain numerous opportunities to exercise and consume foods lower in saturated fats and sugars, suggesting that progression from overweight to obesity is, to a great extent, determined by individual lifestyle choices. As many of the outcomes of compulsive consumption of fast-foods, such as reduction in basal metabolic rate and potential addiction, are largely unknown by many members of contemporary society, it is crucial that this knowledge be made easily accessible in order to heighten individual and community awareness.

**Summing up: The Ethics of Science**

From the biological perspective, health and ill-health are not alternative states; rather they are part of the same continuum where genetic and epigenetic influences sustain, or derail, normal reproductive processes triggering lasting legacies in the next and subsequent generations. As described in this review, we inherit more than just our genes from our ancestors. Inadequate control over the decision-making in one’s life generates a destructive interplay of social, physical, economic and environmental (epigenetic) factors that undermine the determinants shaping the wellbeing continuum. Like all of us, fetuses have mechanisms by which they adapt to deteriorating environmental conditions brought about by parental distress, drug abuse, disease, nutritional excess or deprivation, and non-adaptive lifestyles. In essence, normal development is disrupted by harmful influences and for those surviving their prenatal challenges, the cost maybe a struggle with long-term health consequences [29]. By facilitating information transfer based on biology relevant to contemporary society, future studies will, progressively over time, provide a basis for individual knowledge and the opportunity for the establishment of informed decisions associated with food intake. As obesity is the second most common cause of morbidity and mortality in modern times, it is crucial that further work also focuses upon the fetal origins of obesity and its trans-generational occurrence. Figure 1 allows the reader to see the rapidity of weight increase as measured in some selected OECD countries. The hoped for outcome is that with ready access to ongoing scientific investigations, existing societal mores will change and facilitate informed individual choice supporting the development of a positive foundation to maximize trans-generational health.

![Battle of the bulge](Figure 1: Published in The Weekend Australian Financial Review 9-10 October, 2010, p. 27. (Source: http://economix.blogs.nytimes.com/2010/09/23/the-world-is-fat/)

**References**


