

Review Article

Obesity as Malnutrition: The Role of Capitalism in the Obesity Global Epidemic

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The global obesity epidemic remains poorly understood, partly because it has emerged alongside persisting under-nutrition in many populations. At an abstract level, obesity develops from exposure to the “obesogenic niche,” comprising diverse factors predisposing to weight gain. This article first explores how susceptibility to the obesogenic niche is influenced by developmental and life-history experience. Human growth is sensitive to early-life ecological conditions, under the transducing effect of maternal phenotype. Such plasticity is associated with subsequent variability in body composition and metabolism, impacting susceptibility to the obesogenic niche, albeit with heterogeneity across populations. Both nutritional constraint and nutritional excess during early life are associated with variability in relevant molecular pathways. The article then considers the fundamental contribution of capitalist economics to population under-nutrition and over-nutrition. Historically, capitalism contributed to the under-nutrition of many populations through demand for cheap labor. As the limiting factor for economic growth switched to consumption, capitalism has increasingly driven consumer behavior inducing widespread over-nutrition. In populations undergoing nutritional transition, many individuals encounter both under- and over-nutrition within the life course, elevating both susceptibility and exposure to the obesogenic niche. The interactions between global economic forces and nutritional shifts are distributed across generations, and are strongly transduced by maternal effects. The structural connections between undernourished and overnourished worldwide and between under- and over-nutrition within individual life-courses highlight the central role of capitalist economics in the global obesity epidemic. Prevention policies targeting individual behavior have proved ineffective and economic policies are arguably the optimal target for intervention. *Am. J. Hum. Biol.* 24:261–276, 2012. © 2012 Wiley Periodicals, Inc.

INTRODUCTION

Until late in the 20th century, chronic under-nutrition was the primary human nutritional concern. Within recent decades, obesity has emerged as a new issue of similar global importance. Paradoxically, its rapid increase has not been accompanied by a matching reduction in the prevalence of under-nutrition (FAO, 2011), so that these two nutritional extremes persist alongside each other in many countries, populations, and even families, a scenario known as the “dual burden” (Doak et al., 2000, 2005). Indeed, many individuals show characteristics of both under and over-nutrition within their own phenotype (Popkin et al., 1996, 2001).

Though initially a characteristic of the most industrialized countries, obesity is increasingly common in urban populations throughout Africa, South and East Asia, South and Middle America, Caribbean and Pacific Islands, and indigenous populations living in industrialized countries (Martorell et al., 2000; Popkin, 2003, 2007; Misra and Khurana, 2008). For example, the prevalence of obesity categorized by both body mass index (BMI) and waist-hip ratio exceeded 40% in a recent study of middle-aged urban Indian women (Pandey et al., 2011). Very few countries have achieved much success in obesity prevention programs, and many populations, especially those undergoing rapid modernization, are seeing continued increases in the numbers of those overweight, contributing to increases in chronic degenerative disease risk (Misra and Khurana, 2008; Popkin, 2009).

In industrialized populations, obesity tends to be commoner in those of low socio-economic status (McLaren, 2007; Rosengren and Lissner, 2008). A recent study of countries undergoing economic transition showed that in most, obesity remains most common in those of high

socio-economic status, but that in some, the fastest rate of increase is in those of lower socio-economic status (Jones-Smith et al., 2011). Collectively, these data therefore indicate an ongoing global socio-economic shift in exposure to obesogenic factors, and it is already clear that there is no simple association of obesity with economic “affluence,” either within or across countries (Monteiro et al., 2004a,b; Ezzati et al., 2005).

How can we account for the rapid spread of this state of nutritional excess in such a range of populations, characterized by diverse lifestyles, diets, disease loads, nutritional histories, and genotypes? The dominant explanatory model has long been the energy balance equation, which attributes changes in adiposity (energy stores) to variability in dietary intake or energy expenditure:

$$\Delta \text{energy stores} = \text{energy intake} - \text{energy expenditure}$$

According to this approach, excess weight gain must arrive either from excess energy intake or insufficient energy expenditure, often equated with physical activity (Prentice and Jebb, 1995). A large proportion of obesity research seeks to identify proximate factors associated with excessive dietary intake or inactivity to curtail excess weight gain. Genetic factors also impact obesity susceptibility (Fernandez et al., 2012) but are not addressed in this article.

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Beyond this dominant paradigm, an increasing number of researchers are probing the complex molecular pathways that regulate energy stores and metabolism, and the multi-dimensional nature of the obesogenic environment or “niche” (Keith et al., 2006), as revealed through broader socio-ecological models (Egger and Swinburn, 1997). At an abstract level, exposure to this niche is a prerequisite for increasing obesity prevalence, but individuals and populations may further vary in their susceptibility through diverse underlying mechanisms.

Socio-ecological models of obesity have only rarely addressed the contribution of economic forces and power relations (Albritton, 2009; Chopra and Darnton-Hill, 2004; Wells, 2009a). This review aims to examine the role of capitalist economics in shaping both *susceptibility* and *exposure* to the obesogenic niche. I first review how perturbations in early-life growth interact with subsequent environmental factors to generate variability in obesity risk. Plasticity is proposed to respond to energy availability, resulting in metabolic adaptations which may impact adiposity, and hence obesity risk in contemporary environments. Some of the molecular pathways underlying early growth plasticity and their potential role in excess weight gain following exposure to modern food products are also described. I then discuss the role of global economics in perturbing this physiological plasticity in contrasting directions: the political economy of capitalism has been a long-term significant factor contributing to the poor nutritional status of many populations, but is now further implicated in the systematic over-nutrition of many populations. However, much is discovered about human biology and the behavioral, physiological, and molecular mechanistic basis of obesity, I propose that public health policies are likely to have very limited efficacy if they fail to address these global economic forces.

LIFE-HISTORY PLASTICITY IN GROWTH: TRACKING ENVIRONMENTAL CONDITIONS

Within the “developmental origins of health and disease” (DOHaD) paradigm, much attention has been directed to the life-course etiology of obesity. There is increasing evidence that experience in utero mediated by maternal phenotype is associated with body composition and metabolic phenotype in later life (Armitage et al., 2008; Dabelea et al., 2000; Yajnik, 2004). This has led to interest in the developmental origins of excess weight gain and of variability in associated traits such as appetite and endocrinological profile (Ibanez et al., 2006; Martin-Gronert and Ozanne, 2005). Whether obesity develops in early childhood, adolescence, or adulthood, the fact that early-life factors account for a proportion of subsequent phenotypic variability indicates that a developmental perspective is crucial for understanding the epidemic (Yajnik, 2004). To this end, it is helpful to focus initially on the developmental trajectory of growth and reproductive maturation, rather than on adiposity or obesity itself. As discussed below, plasticity in growth underlies many of the epigenetic or hormonal adaptations that are associated with obesity risk in contemporary environments.

Through such plasticity, early growth responds to ecological conditions, in particular energy availability. Life history theory assumes energy availability to be a key factor regulating trade-offs between survival, growth, immune function, and reproduction (Hill, 1993) and developmental

experience is critical. Classic studies of animals illustrated profound effects of inadequate nutrition in early life on patterns of growth and maturation and reproductive profile (Slonaker and Card, 1923a,b). In humans, signals of reduced energy availability in early life influence the allocation of energy between competing tissues (Hales and Barker, 1992; Latini et al., 2004), whilst also accelerating the schedule of pubertal development (Ibanez et al., 2011; Nettle et al., 2011). These adaptations may be considered complementary: the reduced investment in somatic tissues reduces the chances of survival (Kramer, 1987; Subramanian et al., 2009), and hence favors earlier reproduction.

More generally, growth and maturational schedule may be considered to comprise a process regulated by a series of reaction norms (Stearns, 1992), as shown in Figure 1. For any given genotype, the phenotype that actually emerges is a function of responses to multiple signals of ecological conditions, albeit under transgenerational influence. To some extent, these responses are additive, allowing a degree of plasticity to be maintained throughout the growth process. However, later reaction norms may also be constrained by phenotypic response in earlier windows of development. In particular, early growth has much greater plasticity than later growth in response to nutritional cues. From late infancy onwards, linear growth is canalized (Smith et al., 1976) and variability in nutritional supply primarily affects the rate of development rather than final size.

There are many examples in biology of reaction norms responding directly to external ecological conditions. For example, tadpoles exposed to cues of high mortality risk develop more rapidly, although this response to predation may be mediated by changes in food availability (Chivers et al., 1999; Nicieza, 2000). In some teleost fish, sexual development is responsive to both thermal and social cues (Godwin et al., 2003). In mammals, however, the processes of placental nutrition and lactation insert a buffer between the developing offspring and the external environment and the signals received by the offspring are therefore strongly mediated by maternal phenotype (Kuzawa, 2005; Wells, 2003, 2010).

Figure 2 presents a schematic diagram illustrating how numerous ecological and maternal factors contribute to fetal growth patterns indicating a transgenerational etiology of growth variability. Diverse physical or biosocial environmental factors ultimately act on the fetus through maternal phenotype through a range of physiological mechanisms and regulatory pathways that are still being elucidated. Maternal peri-conceptual nutritional status (Oliver et al., 2005), thermal environment (Wells and Cole, 2002), uterine volume (Kramer, 1987), pregnancy diet (Moses et al., 2006), placental function (Winder et al., 2011), exposure to stress (Harville et al., 2010), pathogens (Ticconi et al., 2003), and physical activity patterns (Schlussel et al., 2008) have all been implicated as mediating mechanisms. A similar scenario persists during the window of lactation, where again maternal physiology transduces the impact of external environmental stresses on the infant (Dewey, 1998; Hinde, 2009; Prentice et al., 1994). I have argued that the periods of maternal physiological mediation and offspring plasticity are closely aligned ensuring that maternal phenotype rather than external ecological conditions is the primary influence on early nutritional adaptation in the offspring (Wells, 2003). Others have also emphasized beneficial maternal influences on offspring developmental plasticity (Kuzawa, 2005,

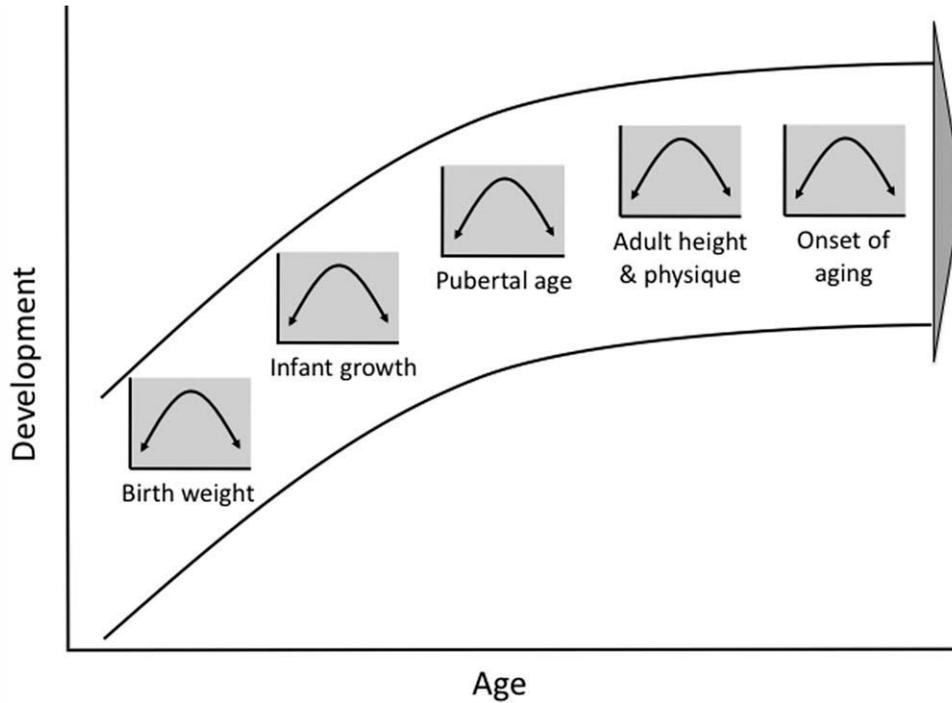


Fig. 1. Life history represented as a developmental succession of reaction norms. At each stage, adaptation is assumed to occur by optimizing phenotype according to signals of ecological conditions represented by fitness peaks for each trait. The relevant signals derive in early life from maternal phenotype rather than directly from the environment. Life history plasticity, and hence fitness peaks, in later traits may be constrained by “decisions” operationalized in earlier reaction norms. Variability in these reaction norm traits has been associated with obesity risk (see Table 1).

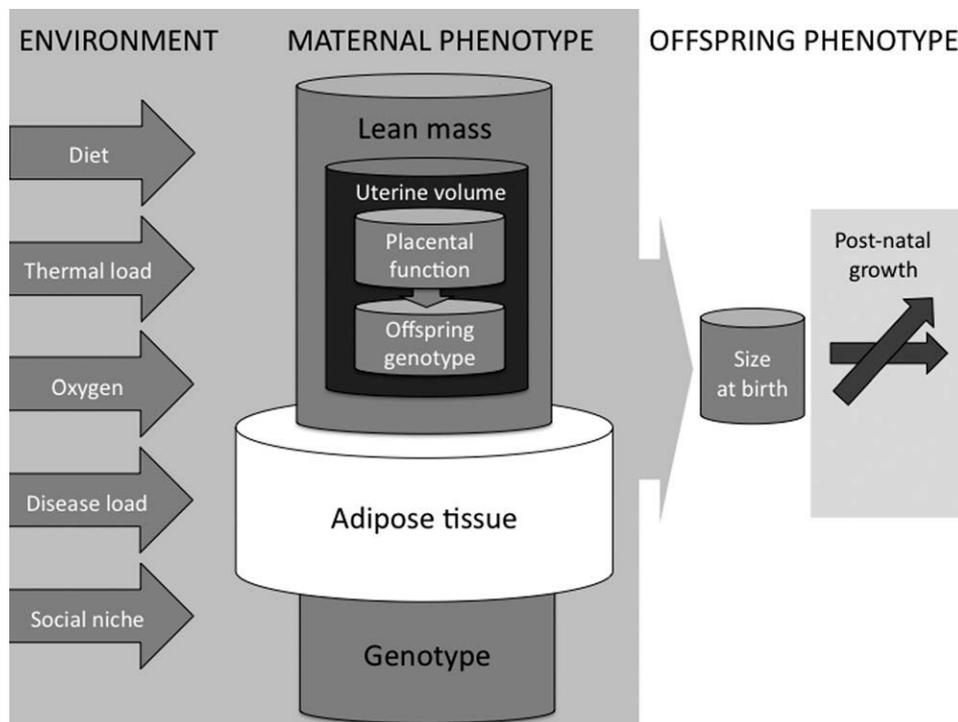


Fig. 2. Factors affecting offspring development transduced through maternal phenotype. Size at birth is a crude outcome measure and does not index all adaptive strategies. However, early growth patterns have been strongly associated with many etiological components of later obesity risk, indicating a key role for developmental trajectory and its interactions with subsequent ecological stresses.

2007). The arguments presented in this article may not necessarily apply equally to all types of developmental cue and are directed to early growth variability and its association with later obesity risk.

There are two things to emphasize about such maternal effects. First, mothers with high quality phenotype can buffer the offspring substantially from a range of ecological stresses as shown by the ability of previously well-nourished women to gestate fetuses during severe famine (Stein et al., 2004). Second, the impact of ecological conditions on a population occurs with a time lag that may operate both within and across generations. Maternal phenotype represents a cumulative index of recent experience including her own development, with short-term perturbations smoothed out to provide a more reliable rating of environmental quality (Wells, 2003). As a woman is born with all her ova already developed, the ova that will form the next generation are influenced by experience in the previous generation (Youngson and Whitelaw, 2008) generating a multi-generational process of phenotypic transmission that is independent of genotype though also potentially interacting with it.

Others have developed a different model of the adaptive nature of early-life plasticity, arguing that it allows offspring development to be targeted at long-term future environments. In the “predictive adaptive response” model, signals received by the fetus are assumed to be used to anticipate the likely conditions in adulthood when reproduction will occur (Gluckman and Hanson, 2004; Gluckman et al., 2007). Specifically in relation to obesity, these authors consider that central adiposity and insulin resistance are adaptations that develop, following fetal under-nutrition, in anticipation of energy scarcity in adult life (Gluckman and Hanson, 2008). A challenge to this approach is that insulin resistance is not present at birth in small babies but rather develops in association with excess weight gain in early childhood (Ibanez et al., 2006), i.e., paradoxically when energy supply is improving.

My approach differs from this anticipatory model by considering growth as a highly dynamic process characterized by competing interests of parents and offspring (Wells, 2003, 2010). The notion of conflicts of interest regarding the transfer of resources from mother to offspring (Haig, 1993; Trivers, 1974) helps understand how successive offspring of a given mother acquire different quantities of investment, reflected in their different growth trajectories and phenotypic quality.

For example, first-born offspring are typically 100–200 g lighter than later-borns (Rosenberg, 1988; Siervo et al., 2010), which may be interpreted as a strategic manipulation of maternal investment across the reproductive career. Early maternal age at first birth and variability in the duration of the inter-birth interval may also influence the magnitude of investment in offspring (Merchant and Martorell, 1988; Thame et al., 1999). According to this perspective, investment in offspring tracks maternal phenotype and maternal reproductive strategy directly and external ecological conditions only indirectly. Small neonates tend to grow faster postnatally (Ong et al., 2000), indicating a counteraction against their initial reduction in maternal investment, hence in some environments, first-born offspring end up on average taller and heavier than their later-born peers despite their smaller size at birth (Ghosh and Bandyopadhyay, 2006; Koziel and Kolodziej, 2001; Siervo et al., 2010; though see Hermanussen

et al., 1988). As discussed below, these variable growth patterns are associated with increased obesity risk in contemporary environments.

This approach emphasizes that early-life plasticity is a complex trait reflecting multiple ecological factors under the umbrella of maternal phenotype. Offspring do not necessarily receive the level of maternal investment that would be optimal for their own future fitness (Karn and Penrose, 1951) rather their allocation of investment represents a compromise between maternal and fetal interests. The benefit to the offspring is that, under natural conditions, the continued influence of a single maternal phenotype throughout pregnancy and the duration of lactation confers homogeneity on the nutritional cues it receives favoring coherent development (Wells, 2003). As discussed below, however, this dynamic sensitivity to maternal cues may increase subsequent susceptibility to the obesogenic niche.

LIFE HISTORY PLASTICITY: ADIPOSITY AS RISK MANAGEMENT

The plasticity in growth described above is associated with different metabolic effects. For example, variability in nutritional supply in utero is associated with variability in infant energy metabolism (Davies et al., 1996) and endocrine profile (Chellakooty et al., 2006; Mericq et al., 2005; Ren and Shen, 2010), and muscle expression of proteins involved in insulin signaling and glucose transport in later life (Vaag et al., 2006). The offspring of obese and diabetic mothers also show metabolic perturbations (Armitage et al., 2008; Vela-Huerta et al., 2008). Many of these metabolic effects have implications for subsequent adiposity, and hence in contemporary environments, obesity risk. Table 1 shows how diverse elements of life history plasticity are associated with subsequent variability in obesity risk.

For example, recent studies have elucidated how reduced birth weight, indicating a lower level of maternal investment, may be associated with a different life history trajectory through to adulthood, involving rapid infant growth, early age at menarche and reduced adult height (Ibanez et al., 2000; Ong et al., 2000, 2009). The potential for such developmental adjustments to persist is demonstrated by a follow-up of 3,743 Scottish women aged ~50 years, showing that earlier menarche remained strongly associated with BMI in middle-age, independent of the influence of childhood BMI (Pierce and Leon, 2005). In western populations, reproduction increases obesity risk, with potential mechanisms including cumulative pregnancy weight gain in women (Harris et al., 1997), and declining testosterone in men (Gray et al., 2002), although lifestyle change may also be important.

Importantly, however, these associations between life history traits and obesity risk are not uniform, and vary between populations. In less developed populations, such as Guatemala, Brazil, and India, several studies have associated rapid infant growth with later lean mass rather than adiposity, although the effects of faster childhood weight gain are more uniform (Li et al., 2003; Sachdev et al., 2005; Wells et al., 2005). Equally, associations between low birth weight and later obesity are inconsistent between populations (Yu et al., 2011). Thus, Table 1 emphasizes that the long-term effects of early growth plasticity on obesity risk appear environment-dependent.

TABLE 1. Associations between life history traits and subsequent obesity risk

	Life course strategy ^a	Association with obesity	Reference
Fetal life			
Low birth weight	Preserves neonatal adiposity in Indians	+ India, 8 years 0 India, 4–17	Bavdekar et al. (1999) Sharma et al. (2007)
Induces rapid infant growth		+ UK, 5 years 0 UK, 10 years	Ong et al. (2000) Rogers et al. (2006)
Primiparity	Induces rapid infant growth	+ Brazil, 18 years (M) + India, 18–21 years (F) 0 UK 18–30 years (M)	Siervo et al. 2010 Ghosh and Bandyopadhyay (2006) Hallal et al., unpublished
Infancy			
Rapid growth	Follows reduced fetal growth	+US African Americans, 20 years + UK, 10 years (F) 0 Brazil, 9 years 0 Guatemala, 21–27 years	Stettler et al. (2003) Ong et al. (2009) Wells et al. (2005) Li et al. (2003)
Formula-feeding	Releases growth from maternal restraint	+ US, 9–14 years 0 US adult women	Gillman et al. (2001) Michels et al. (2007)
Stunting	Favors reduced fat oxidation	+ Brazil, 8–11 years 0 Cameroon, 5 years 0 South Africa 10–15 years	Hoffman et al. (2000) Said Mohamed (2011) Mukuddem-Petersen and Kruger (2004)
Pubertal development			
Early menarche	Follows rapid infant growth	+ UK, ~50 years (F) Finland, 14 and 31 years (F) + India young adults (F)	Pierce and Leon (2005) Laitinen et al. (2001) Sharma et al. (1988)
Adulthood			
Short stature	Follows earlier growth plasticity	+ Germany + Brazil + Serbia + Siberian Buryat (F)	Bosy-Westphal et al. (2009) Ferreira et al. (2009) Pavlica et al. (2010) Leonard et al. (2009)
Reproductive history			
High maternal parity	Cumulative pregnancy weight gain	+ UK (F) 0 Guatemala (F)	Harris et al. (1997) Merchant et al. (1990)
Fatherhood	? declining testosterone, lifestyle change	+ Danish, 20–29 years (M)	Nielsen et al. (2006)

^aProposed life course strategy, as discussed in the text. However, mechanisms may vary within and between populations. + – positive association; 0 – no association; M – male; F – female. Whilst positive associations have been replicated across populations, the evidence is inconsistent, highlighting that associations between early plasticity and later obesity risk are environment-dependent.

To some extent, associations between growth plasticity and subsequent adiposity may be adaptive. Physiological studies have associated adiposity beneficially with many specific life history functions including survival, growth, immune function, and reproduction (Demas et al., 2003; Kuzawa, 1998; Lassek and Gaulin, 2006; Dunger et al., 2006; Pond, 2003). Undernourished individuals with reduced adiposity have poorer growth, lower reproductive success and increased mortality from infectious disease (Wells, 2009a). However, beyond such absolute benefits of energy stores, evidence also increasingly suggests that adiposity *regulates* life history trade-offs, not only supplying the necessary energy for specific functions but also actively contributing to the partitioning of energy supply between them (Wells, 2009b). This is consistent with a recent comparison of mammals, which suggested that large brains and increased energy stores were alternative “solutions” to ecological stochasticity (Navarrete et al., 2011).

Figure 3 represents energy metabolism as an “allocation” game (Wells, 2009b). Incoming calories from food must be either expended on several competing functions or stored in functional tissues or fuel depots. Life-history strategy is then a function of the relative allocation of energy between these competing targets, and developmental experience may affect such allocation decisions. Adipose tissue is involved in a number of key regulatory pathways, in particular that of the hormone insulin, and secretes a number of paracrine and endocrine molecules that moderate insulin metabolism and hence the regulation of growth, reproduction, and immune status (Ahima, 2006). For example, the insulin-sensitizing hormone adi-

ponectin moderates many aspects of reproduction, through receptors in the ovaries, oviduct, endometrium, and testes as well as the central nervous system (Campos et al., 2008; Michalakis and Segars, 2010), and developmental experience contributes to variability in adiponection levels though (Lecke et al., 2011). Adipose tissue also secretes a variety of pro- and anti-inflammatory cytokines as well as diverse growth factors (Atanassova et al., 2007; Badman and Flier, 2007; Permana and Reardon, 2007), so that it is actively involved in both tissue defense and tissue repair. The activity of these signaling molecules is associated with both the quantity and distribution of adipose tissue (Alvehus et al., 2010; Samaras et al., 2010).

Adipose tissue may therefore be considered a sophisticated form of physiological risk management across competing life history functions, orchestrated by a number of signaling molecules that are responsive to early growth patterns (Højbjerg et al., 2011; Ozanne et al., 2006; Vaag et al., 2006). When energy supply is constrained, I hypothesize that the amount and distribution of adipose tissue beneficially regulates competing life history functions, and in doing so reflects developmental experience in interaction with subsequent factors. In obesogenic environments, however, these developmental influences may generate very different outcomes, and thereby contribute to an increased risk of obesity.

MOLECULAR BASIS OF GROWTH PLASTICITY

Mechanistic research on the signaling pathways that enable plasticity in growth and maturation throughout development is critical for understanding life-course vari-

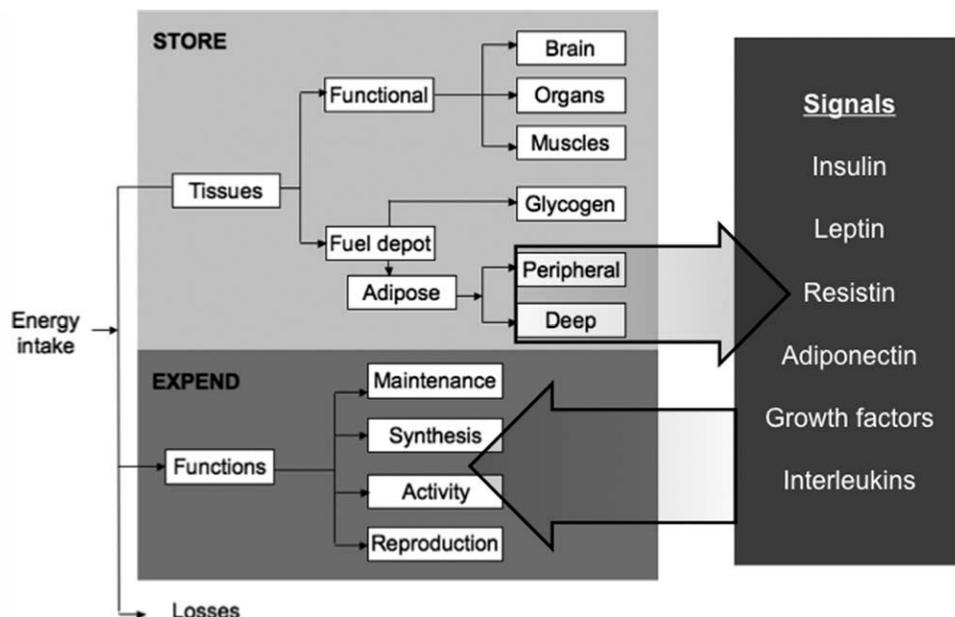


Fig. 3. Energy metabolism as an allocation game. Incoming calories must be either stored in a range of competing tissues or fuel depots or expended on competing life history functions. Adipose tissue not only represents the primary physical store of energy but also secretes a variety of signaling molecules, which interact with other regulatory mechanisms to allocate energy between life history functions. Optimal strategies for storing and using energy are assumed to vary across life-courses, populations, and environments in sex-specific manner, and to be sensitive to developmental experience. Adapted from Wells (2009b).

ability in obesity susceptibility. A comprehensive analysis cannot be presented in this article, however two hormones are particularly important for understanding connections between early growth patterns and obesity risk, namely insulin and IGF1.

When insulin was discovered, it was shown to play a key role in the regulation of blood sugar content (Berson and Yalow, 1965). This has led to a perception that insulin is a hormone of glycemic control. In fact, insulin is involved in myriad metabolic pathways, which affect all life history functions. Insulin is rapidly emerging as a fundamental life history “switch,” playing a key role in the allocation of energy between competing functions and regulating longevity (Harshman and Zera, 2007; Tatar et al., 2003). However, insulin metabolism also integrates the effects of many other hormones, including adipokines (leptin, resistin, adiponectin), growth or sex hormones and satiety factors. In early life, its joint role in nutrient-sensing and growth means that the insulin signaling pathway is fundamental both to early plasticity and to its links with later metabolism and body composition (Hieta-kangas and Cohen, 2009).

Numerous studies have shown that low birth weight babies are born with low levels of IGF1 and insulin (Economides et al., 1991; Ibanez et al., 2009; Randhawa and Cohen, 2005). Soon after birth, however, insulin sensitivity is increased (Iniguez et al., 2010). Studies of both animals and humans suggest that this increased sensitivity is achieved through an increased abundance of insulin and IGF1 receptor proteins in skeletal muscle, favoring faster growth in this tissue (Muhlhauser et al., 2009), and probably in other tissues too, although some of these functional effects appear transient and may be lost by adulthood (Jaquet et al., 2001). Other studies of rodents have demonstrated epigenetic modifications to the IGF1

gene in the liver, in response to the restoration of maternal nutritional status following under-nutrition during pregnancy (Tosh et al., 2010). Importantly, the post-natal upregulation in insulin signaling is mediated by the magnitude of nutritional supply (De Blasio et al., 2007).

Such alterations in insulin metabolism appear central to associations between early growth plasticity and later patterns of lipid accumulation, depending on environmental conditions. However, they are only one example of developmental adaptations to early nutrition which may induce subsequent metabolic responses. More severe post-natal under-nutrition can permanently impair pancreatic beta-cell growth and function, such that glucose tolerance remains impaired even after recovery (James and Coore, 1970; Milner, 1971). Other pathways currently attracting attention include (a) the effect of the hormone leptin on neurons in the arcuate nucleus of the hypothalamus, which plays an important role in appetite regulation through the life-course (Coupe et al., 2009), (b) variability in adipose tissue gene expression (Guan et al., 2005; Lukaszewski et al., 2011), (c) variability in fat oxidation rate which affects metabolic response to diet (Hall et al., 2010; Hoffman et al., 2000), (d) upregulation of IGF1 receptors by formula-feeding (Chellakooty et al., 2006; Larnkjaer et al., 2009), and (e) the effects of antagonistic concentrations of different micronutrients (e.g., low vitamin B12, high folate; Yajnik and Deshmukh, 2008). Some of this research has been conducted on nonhuman animals and requires replicating in humans because the schedule of development varies across species for some components of plasticity. Nevertheless, diverse effects on adiposity and obesity risk have been reported.

The inconsistent associations of life history plasticity and obesity risk illustrated in Table 1 are therefore likely due to heterogeneous transgenerational effects (discussed

further below), interacting with heterogeneous subsequent environmental exposures (e.g., breast- versus formula-feeding during infancy; childhood dietary variability), generating different molecular regulatory effects, and hence varying obesity susceptibility. Thus, while modifications of signaling pathways regulating growth and appetite, often involving epigenetic effects, are likely to prove key to associations between early growth plasticity and later metabolism, much further work is required to understand population variability in these plasticity–obesity associations. Nevertheless, this research is already contributing to our understanding of how broader nutritional trends affect the epidemiology of the obesity epidemic.

METABOLIC RESPONSES TO THE OBESOGENIC NICHE

Despite substantial research, what exactly in the obesogenic niche elicits excess weight gain remains unclear. Although obesity is widely attributed to a failure to regulate energy balance, a recent approach based on complex mathematical modeling attributed the US obesity epidemic to an imbalance of only ~30 kcal/day (Hall et al., 2011), although this may also vary between individuals. Attributing obesity to persistent energy imbalance of small magnitude suggests that neither the gross caloric properties of foods nor broad physical activity trends are the primary contributing factors.

Recently, several scientists have begun to question not the energy-balance equation itself, which is based on physical principles, but the way in which it has been applied in obesity research (Lustig, 2006, 2008; Taubes, 2008; Wells and Siervo, 2011). Perhaps the main limitation of the energy balance equation is that it offers no explanation as to why individuals gain excess weight over time. If an individual consumed 5% more energy than they needed for energy balance on a daily basis, then their weight would initially increase, but it would eventually plateau at a higher body weight once energy expenditure had increased because of the additional body weight. For further weight gain to occur, an additional increase in energy intake would need to occur. Thus, *persistent* weight gain needs *persistent* energy imbalance, a phenomenon that is difficult to understand on the basis of calorie input and output alone (Taubes, 2008).

New approaches to obesity, building on substantial work exploring the metabolic basis of weight regulation, are focusing on the perturbation of cellular energetics. One such hypothesis proposes that diet-induced hyperinsulinemia may play a key role (Lustig, 2006, 2008; Taubes, 2008). Central to this approach is a focus on the role played by fructose, when present either as sucrose (50% fructose, 50% glucose) or as high fructose corn syrup (55% percent fructose, 45% glucose). The combined effect of fructose and glucose metabolism is very different to that of either of them alone. When both are metabolized simultaneously, fructose is converted to triglycerides in the liver, while glucose induces the secretion of insulin. This results in the insulin transporting the triglycerides to adipose tissue depots, and in the process, temporarily inducing a state of “cellular starvation” during which the individual feels both hungry and lethargic (Taubes, 2008).

One type of product strongly associated with both the obesity epidemic (Ludwig et al., 2001; Malik et al., 2006; Vartanian et al., 2007), and with the nutritional transition (Hawkes, 2006), is soft drinks, which have a high content

of sucrose or high fructose corn syrup. Many other processed foods linked with both trends also have a high content of high-fructose corn syrup (Bray et al., 2004). The obesogenic properties of most food products remain a key issue for further research, due to undue attention to their caloric properties rather than their specific effects on appetite and metabolism. However, the evidence linking sucrose-rich products with obesity risk is already strong, including randomized trials (James et al., 2004; Maersk et al., 2012), and these products may play a key role in the global obesity epidemic.

Of particular interest in this article, such foods may interact with adaptations in insulin signaling arising from early growth plasticity described in the previous section, increasing the tendency for excess weight gain. In other words, the early-life adaptations in insulin metabolism that underlie growth plasticity are increasingly implicated in an elevated susceptibility to the obesogenic niche. Although insulin resistance is considered an adaptive element of anticipatory thrift in the predictive adaptive response hypothesis (Gluckman and Hanson, 2004), an alternative perspective considers it to develop as a cellular anti-oxidant stress defense mechanism against insulinogenic diets (Hoehn et al., 2009; Tiganis, 2011), and hence to represent a “coping strategy” rather than an adaptation.

One hypothesis is that the risk of insulin resistance is increased in those experiencing fetal growth constraints because the combination of their low lean mass and upregulated insulin receptors may increase susceptibility to diet-induced anti-oxidant stress in childhood (Wells, 2011). Mitochondrial oxidative stress is considered to play a key role in aging and apoptosis, not least because oxidative damage to mitochondrial DNA is substantially greater than that to nuclear DNA (Sastre et al., 2000a,b). In vitro studies demonstrated that each of insulin, pro-inflammatory cytokines, corticosteroids, and lipid increased mitochondrial superoxide stress, which preceded insulin resistance, and that mitochondrial antioxidant treatment reversed this effect, increasing insulin sensitivity (Hoehn et al., 2009). These findings were replicated in vivo in studies of transgenic mice (Hoehn et al., 2009). A protective role of insulin resistance against mitochondrial damage would help understand why its development in early childhood appears dependent on excess weight gain in childhood, *after* the primary period of catch-up growth when muscle mass can still increase (Ibanez et al., 2006). As formulated in the thrifty phenotype hypothesis (Hales and Barker, 1992), nutritional excess in childhood following early poor growth may be key to the emergence of each of insulin resistance, excess lipogenesis, and chronic inflammation (Alvehus et al., 2010; Berg and Scherer, 2005).

Alterations in insulin signaling are not the only developmental trait that may interact with dietary trends, generating longitudinal associations between early growth variability, and later obesity risk. Other such links include the increasing availability of vegetable oils in middle-income countries, potentially interacting with reduced capacity for fat oxidation (Hall et al., 2010; Hoffman et al., 2000), or with hypothalamic adaptations influencing appetite (Coupe et al., 2009). Such associations are currently the focus on much research across different populations.

The importance of the obesogenic niche in eliciting penalties for earlier plasticity is illustrated clearly if we consider populations not exposed to the niche. Variability in

growth in early life is expected in any population, as shown for example in studies of rural Gambians for birth weight and infant weight gain (Campbell et al., 2003; Prentice et al., 1987). However, in such populations, remaining lean and physically fit into adulthood and consuming a traditional diet, early growth patterns do not predict later insulin profile, and maternal supplementation, which had a modest effect on birth weight, did not affect later body composition or pubertal schedule (Hawkesworth et al., 2008).

So far, this article has discussed progress in scientific understanding of the developmental etiology of obesity susceptibility and in the characteristics of modern dietary products that may activate that susceptibility. Existing data offer a strong message that the association between early plasticity and later health is environment-specific, and that early growth variability does not itself “program” later obesity. Rather, the obesogenic niche is the primary exposure required for obesity, and activates differential susceptibilities that may otherwise remain latent. However, due in part to the influence of the DOHaD paradigm, the scientific community is arguably directing much more attention to studies of early-life plasticity than to the broader environment that elicits the deleterious consequences of early growth variability.

The argument that it is the broader nutritional environment that requires the primary intervention receives less attention from scientists because it involves grappling with political and economic policies rather than the conventional tools of clinical and laboratory science. To address this under-explored area, the final component of this review is to focus on these political and economic phenomena, to improve understanding of how they impose both under-nutrition and over-nutrition unequally across human populations, and hence are fundamental determinants of the obesity epidemic.

“ADAPTATION” AND GLOBAL ECONOMICS: HUMANS AS ECOLOGICAL STRESS

The concept of adaptation has primarily been used in the context of “natural” ecological stresses, such as altitude, temperature, diet, and infectious disease. Paradoxically, little attention has been directed to the fact that the ecological pressures affecting many disadvantaged populations often derive directly from other humans (e.g., Goodman et al., 1988). In the modern world, it is primarily global economic forces that perturb nutritional status within and across generations.

For example, much of the contrast in growth between high and low altitude Andean populations may be due to socio-economic status rather than hypoxia, such that improved living conditions can negate most of the growth deficit (Greksa, 2006; Niermeyer et al., 2009). Such variability in growth is therefore at least partly a response to socio-economic as well as physical environmental factors, yet the word adaptation is rarely invoked in the context of human pressures, even if common physiological mechanisms are involved. This is doubtless because adaptation is generally regarded as a beneficial process whereby the fit of the organism with its environment is “improved,” whereas exposure to chronic poverty is irrefutably a harmful process. In seeking to avoid inadvertent justification of the effects of poverty through reference to “adaptation,” as notably occurred in the case of the “small but

healthy” hypothesis (Seckler, 1982), the fact that humans generate profound long-term effects on each other’s biology slides out of evolutionary view. Only recently have studies of the multi-generational effects of poverty begun to correct this, emphasizing that a proportion of contemporary variation in phenotype can be attributed to socio-economic experience in past generations (Collins et al., 2009; Jasienska, 2009; Varela-Silva et al., 2009). The word adaptation remains relevant to all human phenotypic change over time where lineages persist, but impoverished nutritional status is clearly a suboptimal physiological adaptation when compared with behavioral adaptation, such as social cooperation on strategies for reducing economic inequality.

Evidence increasingly demonstrates that a proportion of human nutritional adaptation has occurred in response to coercive political or economic forces which proactively drive under- or over-nutrition. Contemporary attention inevitably focuses in particular on several dimensions of the capitalist politico-economic model. Through history, however, politico-economic forces have taken many different forms. Evidence from empires throughout the historical period illustrates differential exposure to under-nutrition (Boix and Rosenbluth, 2006). More recently, there is abundant evidence that socialist regimes exposed many amongst their populations to chronic or acute under-nutrition, most notably in the emerging Soviet Union in 1932–1934 and during the “Great Leap Forward” in China in 1958–1961, with estimated deaths of 6 and 38 million people, respectively (Chang and Halliday, 2005; Davies and Wheatcroft, 2004). What distinguishes capitalism in particular is its dominant role in the modern world, its unusual capacity to promote both extremes of nutritional status in large numbers of people, and its increasing capacity to impact simultaneously on people in distant global regions through structural relations of inequality.

Fundamental to my arguments is the notion that capitalism not only exposes many to under-nutrition and others to over-nutrition (Albritton, 2009) but also exposes some to contrasting effects across the life-course. Under- and over-nutrition might be assumed to affect very different populations, yet data on the “dual burden” show us that in populations undergoing nutritional transition, they are typically both present within communities and often within families (Doak et al., 2000, 2005). The stunted overweight individual represents a person who experienced under-nutrition in early life, and over-nutrition subsequently (Bavdekar et al., 1999; Florencio et al., 2001; Popkin et al., 1996). Although over-nutrition is clearly central to the obesity epidemic, the earlier part of this article has further highlighted the contribution of early-life under-nutrition to elevated obesity susceptibility.

HISTORICAL PERSPECTIVE ON CAPITALISM AND NUTRITIONAL PERTURBATIONS

The capacity of capitalism to provoke both nutritional insufficiency and nutritional excess is structurally embedded. Early capitalism in the countries now most industrialized emerged from other aggressively exploitive systems of production such as slavery (Mintz, 1985), and continued to produce profit through the systematic exploitation of labor. In 19th century industrializing populations, the process created a new class of worker, the proletariat who sold his or her labor in return for a wage. Inadequate die-

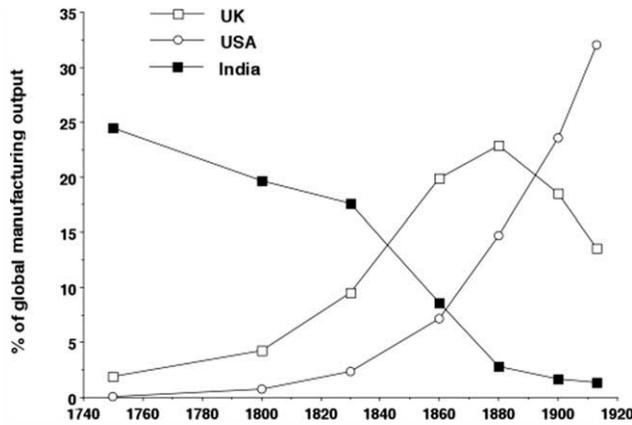


Fig. 4. Share of world manufacturing output according to global regions, based on data from Tomlinson (1990). The decline in the contribution of India is paralleled by increasing output in Europe and the United States, illustrating the structural basis on the contrasting economic fortunes.

tary energy and squalid living conditions reduced the costs of these workers, and therefore boosted profits and the initial pace of industrialization (Albritton, 2009; Hobsbawm, 1968). Adult stature in the UK initially declined during the industrial revolution, and increased primarily during the subsequent century (Komlos, 2008).

By the mid-19th century, however, the pace of industrialization had quickened to the point whereby industrial productivity was no longer invariably the limiting factor for profit. Instead, a second limiting factor had become the size of the market (Hobsbawm, 1968). In Britain, the first country to industrialize, this problem was solved in two ways. First, Britain appropriated overseas markets, forcing its products on other populations and aggressively removing competition (Hobsbawm, 1968; Worsley, 1984). Importantly, this process contributed directly to the worsening nutritional status of overseas populations (Davis, 2002; Rodney, 1972). Second, low wages in the British proletariat were eventually identified as a limiting factor for expansion of the home market, and wages increased to promote consumption (Hobsbawm, 1968). These politico-economic interactions, reproduced in other countries, induced rapid, radical, and connected changes in the living conditions and nutritional experience of populations all around the world, eventually driving each of under- and over-nutrition.

In India, for example, the most “profitable” component of the British Empire, the local textile industry was systematically dismantled, and taxes were imposed to oblige the population to produce crops and raw materials for export back to the metropole (Hobsbawm, 1968). Figure 4 illustrates the dramatic shifts in economic output that derived from these policies. India had been the largest national economy globally at the start of the 18th century, when the UK produced less than 3% of global output, yet by 1870, the average British income was six times that of India or China (Tomlinson, 1990). As the British reorganized the Indian economy for their own benefit, promoting the export of food and cotton, a variety of local Indian institutions that buffered against food insecurity were negated, resulting in appalling levels of famine mortality during a series of El Niño events in the late Victorian era (Davis, 2002). Although height fell in India for millennia,

prior to imperial interactions (Lukacs, 2007), data indicate that male height in India declined at a rate of 1.8 cm per century during the late-colonial period (Ganguly, 1979), indicating a strong link between colonial economic policies and under-nutrition in the Indian population. During the same period, height in England, a recipient of food exported from India, was increasing (Komlos, 1994).

The shift from production to consumption as a limiting factor for capitalist economic development has been played out on a global scale throughout the 20th century. Having already been detached from food production, the urban proletariat were readily converted into consumers (Mintz, 1985), hence urbanization is a key component of consumer society. Global development has been driven forward by the creation of an expanding range of “needs” in western societies (Baudrillard, 1970/1998), affecting food consumption habits in many ways as discussed elsewhere in this issue. More individuals have steadily been drawn into the wage labor workforce, often in export agriculture or industry, and often associated with persisting malnutrition due to loss of control over local food production (Albritton, 2009; Escobar, 1995). A variety of trade liberalizations, supported by improved capacity to transport products around the world, has rapidly increased the reach of the global marketplace whilst increasing inequality in GDP (Bernstein, 2008). These processes have rendered increasing numbers of individuals vulnerable to global efforts to create new consumers in modernizing countries, driven by multi-national food companies and their control over the global production, supply, distribution, and marketing of food (Albritton, 2009).

Figure 5 illustrates traditional and modern shops in Jimma, Ethiopia, where the author contributes to ongoing research on growth and body composition (Andersen et al., 2011). The modern shop, containing almost entirely branded liquids manufactured by multi-national companies and high in oil or refined carbohydrate, epitomizes the efforts to construct a new kind of consumer and hence drive another “emerging market,” in the absence of any coherent effort to address chronic under-nutrition. Local food production in Ethiopia has been reduced in favor of export agriculture, producing coffee and cut-flowers for overseas markets.

Despite being promoted by international organizations specifically to address widespread poverty and malnutrition, the logic of globalized “development economics” has been harshly criticized for addressing the needs of industrialized countries rather than those adopting the recommendations (Chang, 2002; Escobar, 1995). Monoculture cash cropping for export agriculture benefits multinational food companies, at the expense of family food production in those growing the crops, who are then obliged to rely on cheap food imports (Moradi and Baten, 2005; Rosset, 2011). Economic policies driving cheaper food in industrialized populations have contributed directly to over-nutrition in those populations, but also to under-nutrition in others. The structural adjustment programs of the 1980s were associated with increases in low birth weight, malnutrition, and famine mortality in African and South American countries (Christian, 2010; Cornu et al., 1995; Kelly and Buchanan-Smith, 1994; Whiteford, 1993). More recently, in the Asian economic crisis of 1997–1998, declining macronutrient and micronutrient intakes in Indonesia (Hartini et al., 2003) were associated with an increase in maternal chronic energy deficiency and anemia (Block et al., 2004).



Fig. 5. Traditional and modern shops in Jimma, Ethiopia. The modern shop contains almost entirely branded liquid products including soft drinks, widely associated with excess weight gain. The modern shop, but not the traditional shop, has multiple factors favoring over-consumption of calories.

For industrialized populations, the same globalized processes and fiscal austerity transformed the efficiency of food transport systems, reduced the cost of raw materials, and increased consumer buying power (Albritton, 2009). For example, the boom in soy agriculture in Brazil contributed to cheaper and faster livestock-raising in the US, processes that decreased the cost of US meat whilst also raising its fat content (Cordain et al., 2002), though contributing to under-nutrition in Brazil through increase in local food prices (MicMichael, 2005). Growing industrialization of global food production was supported by rapid growth in advertising and the dominance of supermarkets over the food supply system (Chopra and Darnton-Hill, 2004; Shell, 2002), all factors associated with the emergence of the obesity epidemic in western populations, which has occurred primarily in the last three decades (Flegal, 2005; Great Britain Parliament House of Commons Health Committee, 2004).

Coffee offers another potent example of the links between agro-industry, differential nutrition between global regions, and socio-economic inequality. First, coffee is a labor-intensive crop, hence profits are boosted by keeping labor costs low (Albritton, 2009). Plantation workers in many countries have been malnourished for generations, following displacement from their land in the 19th century (Pendergast, 1999). Second, coffee is a major global commodity, subject to volatile market price fluctuations which expose its producers to income insecurity (Bello, 2009; Pendergast, 1999). Third, coffee is heavily marketed in emerging markets to drive broader changes in consumer behavior (Mintz, 1985; Pendergast, 1999). Fourth, coffee is directly implicated in the overconsumption of calories, as caffeine is increasingly added to soft drinks where its presence decreases the perception of sweetness and hence conceals high energy content (Keast et al., 2011) whilst also promoting repeated consumption. Through the unifying logic of capitalism, the tendency for overweight in consumers of caffeinated beverages is structurally connected with the poor nutritional status of coffee producers in other populations. Ironically, coffee itself has little energy content, hence despite its huge scale of production and its powerful role as an agent of economic growth, its contribution to global food security is negligible.

Whilst world food production is now greater than ever before, and the total number of calories is itself adequate for all to be well-nourished (Rosset, 2011), the dominance of the profit motive in the food-industrial complex ensures that many are unable to purchase enough food, whilst others are powerfully steered toward over-consumption (Albritton, 2009). This dual burden of malnutrition has arisen because diverse commercial companies privatize the profits that derive from both under- and over-nutrition, but socialize any costs (Albritton, 2009).

A crucial question is, why is it capitalism that is so closely associated with obesity, rather than other economic systems? A key element of capitalism, which has strengthened substantially in the decades following the second world war, is its role in the loss of individual agency (Mintz, 1985). Commercial organizations have collectively learned to maximize profits through “making consumers” decisions for them. Such decisions are “made” both at the behavioral level, through advertising, price manipulations and restriction of choice, and at the physiological level through the enhancement of addictive properties of foods. For example, sucrose itself can become addictive under some circumstances (Fortuna, 2010; Hoebel et al., 2009), however other addictive substances such as caffeine can also be added to food or beverage products to stimulate repeated consumption (Keast et al., 2011). Loss of agency characterizes not only individuals but also governments and other organizations promoting health. In the 21st century, the food-industrial complex has become so powerful that efforts to re dress the scenario have proved futile (Albritton, 2009) and each of obesity and malnutrition is increasing.

The “nutrition transition” that accompanies rapid economic development is intensifying both under- and over-nutrition, and hence injecting a further dimension of susceptibility into the global obesity epidemic. Figure 6 illustrates the structural connections between nutritional insufficiency and excess, and highlights how the phenomenon of “emerging markets” accelerates the transition between them. Capitalism drives each of under-nutrition in food-insecure populations, over-nutrition in consumer-societies, and the nutritional transition through the logic

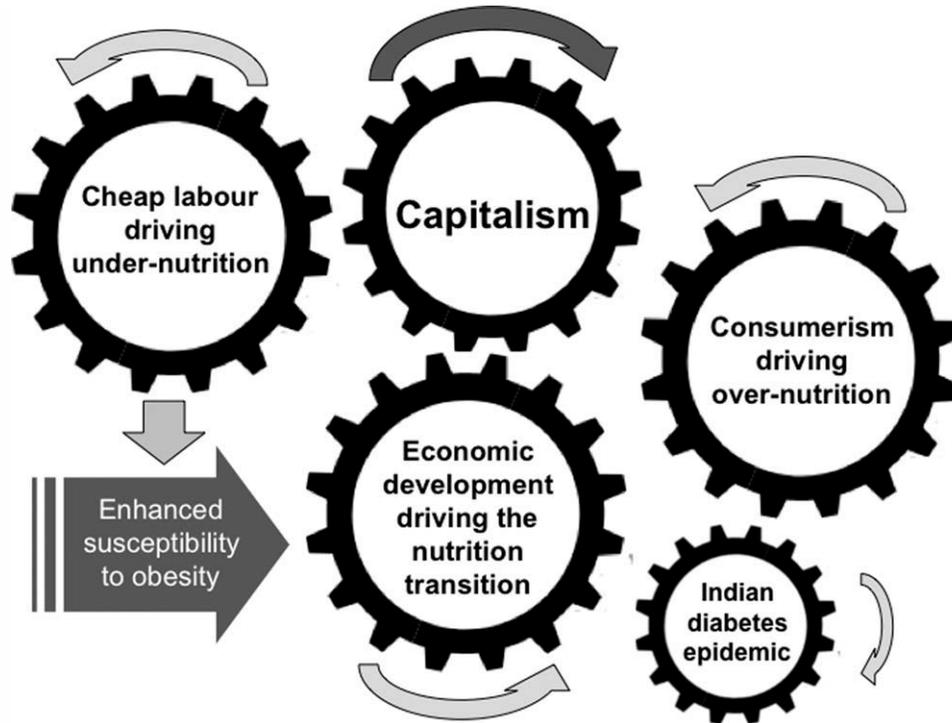


Fig. 6. The structural relationship between contemporary capitalism and malnutrition. The logic of capitalism is portrayed as a cogwheel, integral to the reproduction of each of under- and over-nutrition. For those exposed to “emerging markets,” capitalism further drives a rapid transition between these two nutritional states within the life-course, whilst prior exposure to under-nutrition may exacerbate the susceptibility to obesity in these conditions. The Indian diabetes epidemic represents one example of the composite effect of these different drives.

of globalization. Each of these processes incorporates the loss of agency, through which their adverse effects might otherwise be resisted. Emerging markets are currently considered the primary source of future profits by the food–industrial complex, and are aggressively targeted for expansion. Yet, as reviewed in the first part of this article, a proportion of those individuals newly exposed to the obesogenic niche previously experienced under-nutrition earlier in the life-course, and may have an enhanced susceptibility to obesity. The rapid pace of the nutritional transition maximizes this susceptibility, reflected in the surge in obesity prevalence in such transitioning countries.

Obesity, like under-nutrition, is thus fundamentally a state of malnutrition, in each case promoted by powerful profit-led manipulations of the global supply and quality of food. The speed with which economic forces can change the nutritional status of large numbers of individuals is a key factor in the associated health burden: life-course transitions between under- and over-nutrition are strongly shaped by transgenerational effects, which induce different rates of change in different components of body composition and hence make such rapid nutritional transition more injurious to health.

TRANSGENERATIONAL COMPONENTS OF OBESITY RISK: THE METABOLIC GHETTO

To emphasize the transgenerational component of the association between socio-economic forces and malnutrition, the author proposed the concept of the “metabolic ghetto” (Wells, 2010). Just as the consequences of social marginalization persist across generations (Wirth, 1928),

so the physical effects of malnutrition in one generation propagate forward to subsequent generations, because maternal phenotype represents the dominant developmental niche shaping early life plasticity (Wells, 2003, 2007), as illustrated in Figure 2. Globally, an increasing proportion of offspring may be exposed to maternal malnutrition (whether under- or over-nutrition) before birth, and may transmit some of this legacy on to their own offspring. The emergence of obesity susceptibility may initially go “undetected,” as women who were undernourished during their own development but consuming a high-energy diet during adulthood transmit disordered metabolic effects onto phenotype of the offspring.

The intergenerational transmission of under-nutrition is well-established (Collins, 2009; Varela-Silva et al., 2009; Yajnik, 2009) although different mechanisms may contribute. In India, underweight mothers produce small (thin-fat) offspring who remain undernourished in their own life-course, and repeat the cycle in the next generation (Yajnik, 2009). In UK, one correlate of low birth weight in men born in the 1920s–1930s was a flattened maternal pelvis, indicative of poor nutrition during maternal development (Martyn et al., 1996) and suggesting that health in the 20th century reflected ancestral experience during the industrial revolution.

Such under-nutrition cannot be solved simply by rapid increases in nutritional supply over short periods (Yajnik, 2009). The capacity for energy stores to increase is much greater than the equivalent capacity for stature, which changes primarily across rather than within generations (Wells and Stock, 2011). Sudden increases in population energy intake do not therefore necessarily induce substan-

tial benefits in fetal growth of the next generation, but may rather increase the risk of gestational diabetes in the mother, which imposes its own penalties on the offspring (Yajnik, 2009).

A growing number of studies link maternal obesity in one generation with malnutrition in previous generations. Short maternal stature carries an increased risk of gestational diabetes (Kousta et al. 2000; Krishnaveni et al., 2009; Ogonowski and Miazgowski, 2010; Portha et al., 2011), and the likelihood of this reflecting transgenerational effects of growth plasticity is demonstrated by animal studies (Portha et al., 2011), and by associations in humans of leg length, a marker of early growth status, with gestational diabetes risk (Moses and Mackay, 2004). Work on Pima Indians has shown that maternal onset of diabetes during the life-course significantly increased the risk of diabetes and obesity in the offspring (Dabelea et al., 2000). Substantial data now illustrate the similar adverse impact of maternal obesity on offspring obesity risk (Armitage et al., 2008). A recent study reported an interactive effect, whereby the likelihood of maternal obesity predicting offspring obesity was substantially increased if the mother was born small for gestational age (Cnattingius et al., 2012). Reducing the propagation of malnutrition across generations is therefore a major challenge, in part, because the plasticity relevant to obesity incorporates long-lasting epigenetic effects (Aagaard-Tillery et al., 2008; Tosh et al., 2010).

Furthermore, recent work is suggesting possible mechanisms whereby adult over-nutrition in the maternal generation may contribute directly to the persistence of under-nutrition in the next. For example, obesity in women and children is associated with an increased risk of anemia (Zimmermann et al., 2008), while maternal anemia is associated with low birth weight (Scholl, 2011; van den Broek, 1998). Thus, obesity in one generation may potentially predispose to fetal under-nutrition in the next. The obesity–anemia association appears to be causal, with the inflammatory load of obesity reducing the capacity for iron absorption (Cepeda-Lopez et al., 2011). The hypothetical intergenerational cycle, shown in Figure 7, could potentially apply to other micronutrients besides iron.

This mechanism remains hypothetical and requires further research, but if supported would further strengthen the notion of obesity as malnutrition with multi-generational impact. More generally, it is clear that transgenerational effects play a key role in the global obesity epidemic, and that maternal metabolism represents the primary locus where the detrimental effects of chronic under-nutrition elevate the adverse effects of the obesogenic niche. The hypothesis that changes in nutritional status across the maternal life-span may shape obesity susceptibility of the offspring is therefore a key area for further research.

DIRECTIONS FOR FUTURE WORK

In this article, I have focused on two fundamental associations in which capitalism is structurally implicated in the obesity epidemic: one the one hand, a global connection between the under-nutrition of some and the over-nutrition of others, each process deriving from the maximization of profit at the expense of individual health; and on the other hand, a life-course association between early under-nutrition and later over-nutrition, following exposure to global economic expansion, which drives the

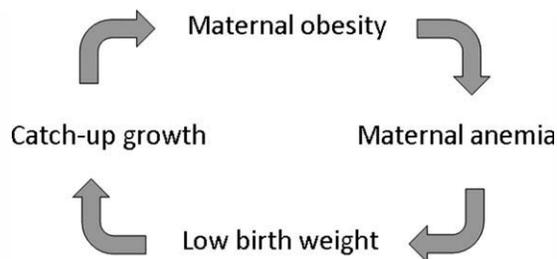


Fig. 7. A proposed intergenerational cycle, based on a link between maternal obesity and reduced birth weight in the next generation, predisposing to catch-up growth in the offspring with increased obesity risk. Recent research suggests that the inflammatory load of obesity reduces iron absorption (Cepeda-Lopez et al., 2011), predisposing to maternal anemia (Zimmermann et al., 2008) and hence potentially to low birth weight. This hypothesis merits testing to clarify the malnutrition status of obesity.

“nutritional transition.” According to this perspective, capitalist economics shapes both *susceptibility* and *exposure* to the obesogenic niche. Elucidating relevant biological mechanisms is crucial for improving understanding of the links between global economics and the obesity epidemic.

At the physiological level, some of the mechanisms underlying differential obesity susceptibility are emerging, but the evidence base remains poor. The generic hypothesis that early-life plasticity is associated with later obesity risk merits further work in different populations, to establish population-specific risk factors. Key issues include:

- Understanding how specific foods or behaviors perturb cellular energetics.
- Establishing the heterogeneous physiological mechanisms whereby susceptibility to obesity is increased.
- Elucidating the biology of multi-generational trends from under- to over-nutrition.
- Assessing the potential mechanisms and timescale of reversibility of such environmental effects, for example, to break the cycle of transmission in those already obese.

Such research would clarify the developmental etiology of obesity risk and its potential for modification or reversal, and public health progress can undoubtedly be made through these activities.

However, whilst research on susceptibility is important, the primary factor causal to obesity is the obesogenic niche itself. Given the broader-scale economic effects discussed above, obesity policies focused on individual responsibility are unlikely to be effective at addressing the epidemic. The obesogenic niche may be considered a “toxic” environment (Poston and Foreyt, 1999; Wells, 2009a), and should arguably be the primary target of obesity interventions. The most serious dimension of capitalist economics is its potential for mass imposition of under- or over-nutrition on large numbers of individuals over brief time periods. A second key area for further research is therefore to understand how to address broader social and economic forces. In this context, key issues include:

- Reorganizing the global agricultural system to increase the equitable distribution of nutritious food.

- Developing public health policies for reducing under-nutrition that do not elevate obesity risk.
- Restructuring global economic development to reduce chronic disease risk.
- Developing effective approaches for regulating commercial interests.

These issues are clearly broad-scale and ambitious, but have substantial conceptual and material overlap with emerging approaches for dealing with climate change (Costello et al., 2011; Egger, 2011; Wells, 2009a), offering important opportunities for convergent solutions. Increasing individual agency is likely to be central to each of these aims. Human biologists and anthropologists have a major role to play in this study, as they can contribute unique expertise regarding the link between behavior and biology, and regarding the challenge that solutions are likely to work across rather than within generations.

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