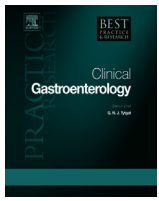
Best Practice & Research Clinical Gastroenterology 28 (2014) 533–544

Contents lists available at ScienceDirect

Best Practice & Research Clinical Gastroenterology



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The aetiology of obesity beyond eating more and exercising less

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Keywords:
Obesity
Drug-related side effects and adverse reactions
Sleep
Infection
Microbiota
Reproduction
Endocrine disruptors
Epigenomics
Smoking
Temperature

A B S T R A C T

Although recent increases in availability of energy dense, processed foods and reductions in institutionally driven physical activity have created an environment that is permissible for obesity to occur, several other factors may contribute to the development of obesity in this context. We review evidence for eleven such factors: endocrine disruptors, intrauterine effects, epigenetics, maternal age, differential fecundity and assortative mating by body mass index, microorganisms, reduction in variability of ambient temperatures, smoking cessation, sleep debt, and pharmaceutical iatrogenesis. Evidence for the role of endocrine disruptors, microorganisms, ambient temperatures, sleep and reproductive factors is accumulating, but additional research is needed to confirm the causative role of these factors in human obesity. However, the role of certain pharmaceuticals and smoking cessation in development of human obesity is clear. Practice points for consideration and future research needed are highlighted for each factor.

Introduction

The obesity epidemic is considered one of the biggest public health concerns facing developed countries across the globe. However, the causes of obesity are not well understood. When energy

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http://dx.doi.org/10.1016/j.bpg.2014.07.001
1521-6918/

intake exceeds energy expenditure, the excess energy is stored, often as body fat. This well documented phenomenon has purported the idea that obesity is caused by recent increases in the availability of energy-dense food, and changes in built environments and institutionalized physical activity, which create an 'obesogenic' environment. Although energy intake must exceed energy expenditure to result in weight gain, and 'obesogenic' environments are permissive for this to occur, they are not always necessary or sufficient to cause obesity. An individual can become obese in the absence of an 'obesogenic' environment, and an individual does not necessarily become obese in an 'obesogenic' environment, suggesting other factors may play a role. Herein, we describe eleven additional factors that may contribute to obesity.

Endocrine disruptors

Chemicals that mimic the effect of hormones if ingested or absorbed in the body are known as endocrine disruptors (EDs). Pesticides such as tributylin (TBT) and organophosphate or organochloride containing compounds (dichlorodiphenyltrichloroethane (DDT)), flame retardants such as polybrominated diphenyl ether (PBDE), plasticizers such as Bisphenol A (BPA) and phthalates, compounds used in non-stick coatings such as perflouroalkyl sulfonate and perfluorooctanoic acid (PFOA), and polychlorinated biphenols (PCBs) used in electronics have been studied as possible contributors to obesity [1]. Of these, PCPs, PBDE, and DDT are persistent organic pollutants (POPs) that have high bioaccumulation and exposure potential. Other EDs such as BPA, Phthalates, and PBDE are less persistent in the environment, but are produced in high volumes, and exposure is nearly ubiquitous [2]. Route and degree of exposure to EDs varies depending on the chemical [1].

EDs may act by inducing adipogenesis [3], altering sex hormone metabolism [4], or foetal development. Exposure to EDs causes obesity in some animal models, and that exposure during critical developmental stages may be important for this effect [5,6]. Perinatal exposure to BPA does not consistently produce obesity [6–8], and its effects may be dose, developmental period, and sex-specific. Perinatal PCB and TBT exposure causes obesity in rodent models [5].

Epidemiological associations between ED exposure and obesity in humans have been reported [9]. The association of obesity with DDE, a DDT metabolite, is fairly consistent, but the association of other EDs such as PCB, PCBE, and BPA is less consistent and appears to depend on dose, developmental stage of exposure, and follow-up time. Fat-soluble organochlorine compounds leak into the bloodstream following weight loss, and this is associated with changes in T(3) levels and is hypothesized to possibly play a role in reduced resting metabolic rate and weight regain following weight loss [10,11]. Thus, there is evidence that some EDs may be associated with human obesity, but a more systematic examination of the longitudinal effects of exposure dose, timing of exposure, and long-term consequences on body fatness are needed.

Reproductive factors

Intrauterine effects

The intrauterine environment influences development of the foetus. Plasticity during gestational development is crucial for adapting the foetus to its anticipated environment. Matching of the foetus' energy requirements to the energy availability in the anticipated environment is particularly crucial with respect to the development of obesity.

A nutrient-deprived intrauterine environment influences offspring body fatness in animals, and the effect may be exaggerated if the offspring are exposed to a high-fat diet post-weaning [12]. Offspring of nutrient-deprived mothers have greater preference for high fat diets and are more sedentary [12]. Findings from the Dutch famine suggest nutrient deprivation during the first trimester may be particularly impactful on obesity outcomes relative to later in pregnancy [13,14]. Maternal leptin levels may be a key factor regulating this response since leptin administration protects offspring of undernourished mothers from these outcomes [15].

Conversely, animal studies suggest maternal over nutrition may influence offspring outcomes. Maternal high fat diet in mice produces hyperphagic offspring with greater fat mass, and reduced