Obesogens


PROF. RENALD BLUNDELL


DR JEAN CLAUDE GRECH

Obesity is a multifactorial disease, leading to adverse health outcomes. Being on a steady increase around the world, obesity has become the new pandemic affecting people's lives across all ages. An individual is considered as obese if the excessive weight is likely to cause a health risk that can be detrimental to that individual. A number of studies suggest that obesity is not only caused by poor eating behaviours or lack of physical activity, but also through chemicals found in commonly used items, scientifically referred to as obesogens.

Obesity

Obesity is commonly measured using the Body Mass Index (BMI), calculated using the person's weight and height, as well as the waist-to-hip ratio. In BMI, obesity is categorised into three classes: Obesity Class 1: BMI 30 to 34.9; Obesity Class 2: BMI 35 to 39.9 and Obesity Class 3: BMI 40 or more. Nonetheless, both BMI as well as waist-to-hip ratio are only screening tools, and not diagnostic tools, to estimate weight status in relation to potential disease risk. In fact, since BMI does not differentiate between fat mass and lean mass, individuals with high muscle mass, such as athletes, may have high BMI but low body fat percentage, leading to a misclassification of their weight status. Delving deeper into understanding the complexities of obesity, it is becoming increasingly evident that environmental factors, particularly the presence of obesogens, play a significant role in weight regulation.

What are obesogens?

Obesogens are endocrine disrupting chemicals that can promote obesity by interfering with the metabolism and hormones that control weight, particularly those related to appetite control and fat storage such as insulin, thyroid hormones and sex hormones. In a nutshell, obesogens can cause weight gain by altering lipid homeostasis to promote adipogenesis and lipid accumulation, and this may occur by multiple mechanisms, including the following: increasing the number of fat cells (adipocytes), increasing the size of fat cells and/or increasing the storage of fat per cell. It may also alter endocrine pathways responsible for control of adipose tissue (body fat) development, alter hormones that regulate appetite, satiety, and food preferences, alter basal metabolic rate, alter energy balance to favour storage of calories as well as alter insulin sensitivity and lipid metabolism in endocrine tissues such as pancreas, adipose tissue, liver, gastrointestinal tract, brain and muscle.

Where are obesogens in everyday life?

Obesogens are found in various commonly used items, such as food containers, cookware and other household items, personal care products as well as industrial, consumer and medical products such as electronics. However, they may also be found in food, air and water, especially in contaminated sources and polluted areas which have increased exposure to obesogens. Some examples of obesogens include Bisphenol A (BPA), commonly found in the lining of food cans; phthalates, widely used in personal-care products such as soaps and shampoos; perfluorooctanoic acid (PFOA), a chemical which has historically been used in the production of non-stick pans, as well as certain pesticides widely used in agriculture. There are also naturally occurring obesogens, such as fructose, which is a sugar found in fruits and honey.

Humans interact with obesogens on a daily basis, both intentionally and unintentionally, at work, school and at home. They are an unnecessary potential hazard to health which can have a large impact on how individuals gain and lose weight and, although preventable, studies show that certain obesogens, such as BPA, are able to seep into the body even just by handling products made from it.

Exposure to obesogens during critical periods of development, such as prenatal or early childhood stages, is of particular concern as it may have long-term effects on weight regulation and metabolic health due to predisposing the body to store higher amounts of fat. In this regard, some studies found a strong association between maternal smoking and childhood overweight/obesity, due to nicotine being an obesogen.

Obesogens and their associated medical conditions

Despite the fact that research on obesogens is still evolving, there is evidence relating the exposure of these chemicals to several medical conditions which can be detrimental to the health of the individual. These include obesity, type 2 diabetes mellitus, cardiovascular diseases, metabolic syndrome, non-alcoholic fatty liver disease (NAFLD), reproductive disorders, neurological disorders and cancer.

These medical conditions could also be directly associated with obesity itself. Obesity has shown to increase the risk of cancer, including breast, liver, colon and ovarian cancer. In fact, according to the Centres for Disease Control and Prevention, 40% of newly-diagnosed cancers each year are associated with obesity. Research has found that obesogens may increase the risk of cancer particularly in hormone-related cancers, such as breast and prostate cancer. Obesity is also a significant risk factor for type 2 diabetes mellitus. Obesogens are found to increase the risk by enhancing the resistance of insulin and as a result impairing the metabolism of glucose. The resistance of insulin occurs when the cells in the human body become less reactive and responsive to the effect of the insulin which lowers the blood glucose levels, hence leading to elevated blood glucose levels known as hyperglycaemia. Gradually, the high blood glucose in the blood can potentially affect other organs including the heart, kidney as well as the eyes.

In relation to cardiovascular diseases such as hypertension, heart disease and stroke, obesogens may contribute to the development of these conditions through their effects on obesity and metabolic dysfunction. In addition, obesogens are also implicated in the development of metabolic syndrome, that is a cluster of conditions that incorporates obesity, high blood pressure, high blood sugar, abnormal lipid levels and resistance to insulin, further increasing the risk of development and progression of cardiovascular diseases. They are also associated with non-alcoholic fatty liver disease by promoting the accumulation of fat in the liver leading to non-alcoholic fatty liver disease. NAFLD can eventually progress to more severe liver conditions, including non-alcoholic steatohepatitis (NASH) and cirrhosis.

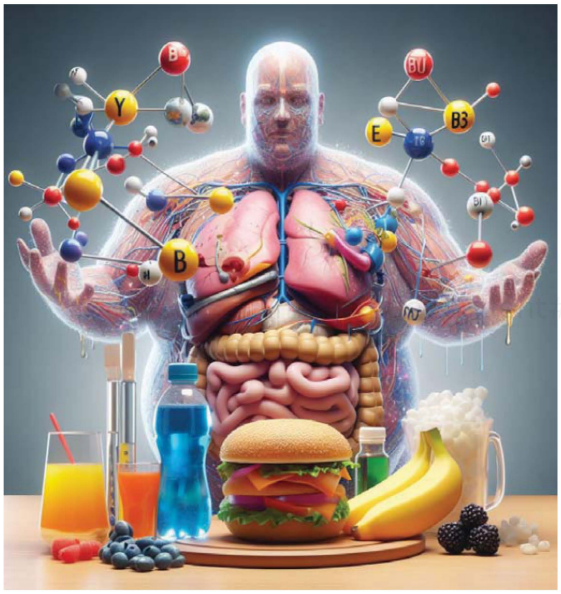
Evidence also suggests that obesity may also have implications for neurological disorders due to affecting the structure and function of the blood-brain barrier (BBB). Such disorders may include Autism spectrum disorders and Attention deficit hyperactivity disorder (ADHD) as well as Alzheimer's. Furthermore, due to their disruptions in hormone signalling pathways, obesity and obesogens are also associated with reproductive disorders including polycystic ovary syndrome (PCOS), menstrual irregularities and infertility.

Mechanism of action

There are many ways in which obesogenic drugs and chemicals can disrupt the body's adipose tissue biology. The three main mechanisms of action are: (1) Central balance of energy, (2) Metabolic sensors and (3) Sex steroid dysregulation.

Central balance of energy

In the brain the HPA axis (hypothalamic-pituitary-adrenal) is involved in controlling appetite and energy homeostasis circuits which are mediated by a large number of monoaminergic, peptidergic (use



of hormones as neurotransmitters) and endocannabinoid signals that come from the digestive tract, adipose tissues and from within the brain. It is through these types of signals that provide a likely target for obesogens, leading to possible weight altering effects. Several hormone pathways within the brain that control appetite and energy balance such as ghrelin, neuropeptide Y, are specifically sensitive to changes in nuclear receptor signalling pathways and can therefore be easily altered by the introduction of endocrine disruptors such as obesogens. Such an alteration can lead to induced feelings of hunger and decreased feelings of fullness, causing an increase in food intake and inability to feel satisfied, hence leading to obesity.

Metabolic sensors

In the hypothalamus there are regions, known as metabolic setpoints, that control the responses that establish metabolic efficiency of an individual. These responses have shown to adapt according to the needs of the individual and their job is to restore the metabolic setpoint by increasing or decreasing the metabolic functions depending on the energy needs of the individual. Due to the persistence of obesogenic phenotypes, the adaptive response components of the hypothalamus are impacted, resulting in an impact on the metabolic efficiency and hence on weight.

Sex steroid dysregulation

Sex steroids are crucial when it comes to lipid balance in the human body. This is aided by other hormones including growth hormones that act against lipid accumulation mediated by insulin and cortisol by mobilizing lipid stores that are present. Exposure to obesogens often leads to a deficiency or change in the ratio between androgen and oestrogen sex steroid levels, which changes this method of lipid balance resulting in lowered growth hormone secretion, hypocortisolaemia (low levels of circulating cortisol) and increased resistance to insulin effects. This alteration in sex steroid levels due to obesogens can vary enormously according to both the sex of the exposed individual as well as the timing of the exposure. If the chemicals are introduced at critical period of development, the vulnerability of an individual to their effects is much higher than if exposure occurs later in adulthood.

Minimising exposure to obesogens

Various strategies may be implemented to reduce exposure to obesogens, most of which revolve around being cautious on what is purchased and consumed. This may be done through choosing fresh and minimally-processed foods over packaged, canned or highly-processed foods to reduce exposure to obesogens like BPA and phthalates, filtering tap water prior to drinking to minimise consumption of perfluorooctanoic acids and phthalates, using natural personal care and cleaning products and being cautious when purchasing household items, especially cookware, furniture and electronics, and ventilating indoor spaces especially after usage of paints, varnishes and cleaning products.

In recent years advocates for policies that restrict the use of obesogenic chemicals in consumer products and promote safer alternatives have led to companies specifying when their products are BPA-free, phthalate-free, PFOA-free, among other labels which indicate that a product is environmentally-friendly or non-toxic. By looking for such labels when making purchasing decisions, individuals can reduce their exposure to obesogens and mitigate potential health risks associated with these chemicals.

Renald Blundell is a biochemist and biotechnologist with a special interest in Natural and Alternative Medicine. He is a professor at the Faculty of Medicine and Surgery, University of Malta

Jean Claude Grech is a medical doctor at Mater Dei Hospital