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# Environmental pollutants and the obesity: proven causalities and open questions

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## Abstract

The link between environmental pollution and obesity is of high importance, because understanding the relationship between the two can provide valuable insights into the complex factors contributing to the obesity epidemic. These chemicals, termed "obesogens," are believed to disrupt lipid metabolism processes, therefore promoting the development of obesity. Human activities such as industrialization, urbanization, agriculture, and transportation have significantly contributed to environmental pollution. Therefore, the main identified obesogens are BPA found in plastics, food packaging, and thermal paper receipts, phthalates, commonly used in plastics, personal care products, and food packaging, toxic metal(oid)s, determined in non-stick cookware, water-resistant fabrics, and food packaging, pesticides, used in agriculture, as well as other persistent organic pollutants (POPs), and pharmaceuticals (waste). Addressing environmental

pollution not only has the potential to improve environmental quality, but also to promote public health and prevent obesity-related diseases. Addressing the causality between pollutants and obesity could be a new and challenging road map for health professionals.

**Key words:** obesity, plastics, metals, POPs, pharmaceuticals, road map

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## Introduction

The World Health Organization (WHO) has identified obesity as a major public health concern. Obesity can be considered a pandemic due to its widespread prevalence across different countries and populations (1). As defined by the WHO, obesity is characterized by an abnormal or excessive accumulation of body fat, which poses potential health risks. This condition is typically assessed using Body Mass Index (BMI) criteria given by the WHO: a BMI over 25 is considered overweight, and over 30 obese. In children aged 5–19 years, being overweight means having a BMI-for-age greater than 1 standard deviation above the WHO Growth Reference median; and obesity is greater than 2 standard deviations above the WHO Growth Reference median (1, 2). Factors like overeating, sedentary behavior, and genetic predispositions are commonly associated with obesity. However, they do not fully explain the recently observed significant rise in obesity rates and associated health problems (3 – 9).

### The development of obesity

The development of obesity involves physiological mechanisms that regulate energy balance, metabolism, and fat storage in the body (1). One key mechanism in the development of obesity is the imbalance between energy intake and energy consumption. When individuals consume more calories than their bodies require for daily activities and metabolic processes, the excess energy is stored as fat, leading to a weight gain over time. Hormones such as leptin and ghrelin are responsible for appetite and energy balance. Leptin, produced by fat cells, signals the brain to reduce food intake and increase energy expenditure when there is sufficient fat stored. Conversely, ghrelin stimulates hunger and promotes food intake. Insulin plays a role in obesity by regulating blood sugar levels. Insulin resistance, a condition in which cells become less responsive to insulin, can increase fat storage and contribute to obesity (8, 10, 11).

Inflammation and oxidative stress are also implicated in the pathophysiology of obesity. Adipose tissue, or fat cells, secretes pro-inflammatory molecules that can disrupt metabolic processes and promote insulin resistance, further exacerbating weight gain. Genetic factors can predispose individuals to obesity by influencing metabolism, fat distribution, and appetite regulation. Environmental factors, such as diet, physical activity levels, and exposure to obesogenic chemicals, also play significant roles in the development of obesity (1, 11).

### Environmental pollutants and obesity: it is time for health professionals

There is increasing evidence suggesting a link between environmental pollutants exposure and obesity (1, 3, 4, 8, 12-17). These chemicals, termed “obesogens,” are believed to disrupt lipid metabolism processes, therefore promoting the development of obesity (12, 16-18). Moreover, environmental pollutants have been shown to disrupt the endocrine system and metabolism, which could also lead to weight gain and obesity (10, 19-23). Obesogens could be found in numerous sources such as plastics, metal(oid)s,

pesticides, as well as pharmaceuticals and industrial chemicals present in the air, water, and ground as a result of intentional or unintentional a1nthropogenic activities (9, 24).

The mechanisms of environmental pollutants that contribute to obesity genesis include disruption of hormonal signalling, affecting metabolic processes including fat storage and appetite regulation; altered gene expression; adipogenesis; inflammation, etc. (8). For example, chronic exposure to certain chemicals found in plastics may promote mild inflammation, which is a step towards obesity and related metabolic disorders (1, 8, 14).

**What are the costs of obesity?**

In Europe, direct and indirect costs associated with overweight and obesity represent approximately 0.47–0.61% of the GDP. In the US, the projected annual health expenses per obese individual were estimated at $1,901 in 2014, resulting in a national extrapolated cost of $149.4 billion. Therefore, investment in reducing exposure to obesogens could be a strategy for the prevention of overweight and obesity and healthcare system savings (1, 25).

**How much and why is the environment polluted?**

Human activities such as industrialization, urbanization, agriculture, and transportation have significantly contributed to environmental pollution. These activities release a wide range of pollutants into the air, water, and soil, leading to environmental degradation. Industrial processes, including the burning of fossil fuels, chemical manufacturing, and waste disposal, release pollutants such as carbon dioxide, sulfur dioxide, nitrogen oxides, heavy metals, and volatile organic compounds into the atmosphere. These pollutants contribute to air pollution, smog formation, and climate change. Agricultural practices, such as the use of pesticides, fertilizers, and livestock farming, can lead to water pollution through a runoff of chemicals into rivers, lakes, and seas. This pollution can harm aquatic ecosystems, contaminate drinking water sources, and affect human health. Urbanization and transportation activities generate pollutants such as particulate matter, nitrogen dioxide, and carbon monoxide, which contribute to air pollution in urban areas. The accumulation of pollutants in the air can have detrimental effects on respiratory health and overall well-being. Natural processes, such as volcanic eruptions, wildfires, and biogenic emissions, also contribute to environmental pollution. However, human activities have significantly amplified the levels of pollutants in the environment, leading to widespread pollution and its associated impacts on ecosystems and human health (26-28).

**Concerns: BPA, phthalates, metals, pesticides, POPs, pharmaceutical waste**

Some of the most important obesogens that have been identified in research include BPA found in plastics, food packaging, and thermal paper receipts, phthalates, commonly used in plastics, personal care products, and food packaging, toxic metal(oid)s, pesticides,

used in agriculture, as well as other persistent organic pollutants (POPs) and pharmaceuticals (waste) (4, 6, 8, 12-15, 17, 29, 30).

Plastic constituents are one of the causes of obesity. There is evidence of correlation and a proven dose-response relationship between chemicals that have migrated from plastics and obesity. BisphenolA (BPA) and phthalates (plasticizers) have been linked to endocrine disruptions, either mimicking the hormones or interfering with hormone signalling pathways (14, 15). Furthermore, plastic constituents may also impact the gut microbiome, which plays a crucial role in regulating metabolism and energy balance and could potentially be associated with obesity (7, 23, 31). Investing in raising awareness of the need to reduce the use of plastics and recycling could support the aforementioned prevention measures (3).

The relationship between metal exposure and obesity is a complex and multifaceted issue that is still being studied. Metal(oid)s such as lead, cadmium, mercury, and arsenic are known to be toxic to humans and have been associated with various health effects, including obesity (4, 8, 17). Exposure to metal(oid)s has been linked to inflammation, oxidative stress, and hormonal imbalances, factors involved in the etiology and pathogenesis of obesity (29, 30). Lead exposure has been shown to interfere with insulin signalling and glucose metabolism, potentially leading to insulin resistance and weight gain (29, 30). Chronic exposure to metals may also impact the gut microbiome, which plays an important role in regulating metabolism and energy balance (32). Overall, reducing exposure to toxic metals through occupational safety measures or dietary choices may be important in mitigating the potential health risks associated with metal exposure, including obesity.

Pesticides are chemicals used in agriculture to control pests and increase crop yields. Some pesticides have been identified as potential obesogens, meaning they may disrupt the endocrine system and metabolism, leading to weight gain and obesity (5).

The findings of the study of Noppakun and Juntarawijit (2022) indicate a strong association between many pesticides and the prevalence of obesity (33). Among the 35 individual pesticides surveyed, 22 showed significant associations with obesity. These included the herbicide butachlor, 15 insecticides (two carbamates - carbaryl, carbosulfan; five organochlorine insecticides - endosulfan, dieldrin, aldrin, DDT, chlordane; and eight organophosphate insecticides - abamectin, chlorpyrifos, methamidophos, monocrotophos, mevinphos, dicrotophos, dichlorvos, profenofos), and six fungicides (metalaxyl, propineb, carbendazim, thiophanate, benomyl, bordeaux mixture) (33). In the same study, the authors discussed the function of some pesticides as endocrine-disrupting chemicals (EDCs). Namely, EDCs interfere with hormone action and act as obesogens, improperly regulating lipid metabolism and adipogenesis to promote obesity. Moreover, EDCs affect weight gain by altering lipid metabolism, fat cell size and number, and hormones involved in the appetite, food preference, and energy metabolism (33). Additionally, some pesticides have been shown to induce inflammation and oxidative stress in the body, which can contribute to metabolic dysfunction and insulin resistance, both of which are associated with obesity. Currently, there are 105 pesticides listed as

EDCs, including insecticides (46%), such as OCs DDT, 2,4-D, aldrin, endosulfan, and chlorpyrifos; herbicides (21%), such as alachlor, diuron, and glyphosate; and fungicides (31%), such as benomyl and carbendazim (33).

Aaseth et al. (2022) discussed POPs as potential obesogens capable of impacting adipose tissue development and function, thereby potentially contributing to obesity (12). The authors jointly considered the evidence from experimental studies that demonstrates that POPs could interfere with obesity by disruption of adipogenesis regulators such as PPARγ and C/EBPα, interaction with nuclear receptors, induction of epigenetic alterations; and/or elicitation of proinflammatory responses (12). Findings from *in vitro* and *in vivo* experiments, considered jointly, point to the impact of POPs on adipogenesis, which is influenced by biological variables such as sex, age, and duration of exposure (12). Some of the most common applications of per- and polyfluoroalkyl substances (PFAS), chemicals that belong to POPs, included pesticide formulation, firefighting foams, cosmetics, aviation, aerospace and automotive industries, textiles coating, oil production, medical products, food processing, building and construction, energy, paper and packaging, cables and wiring, electronic and semiconductors (24). Because of their high persistency and extremely low biodegradability, PFAS are ubiquitously present, leading regulatory agency to consider a decision on the ban of production, placing on the market and use of these chemicals, nowadays recognized as environmental pollutants (24).

An upcoming environmental challenge has already been recognized in pharmaceuticals and their waste. Sharma et al. explained that pharmaceuticals use is increased globally, and a further increase could be expected because of longer life expectancy and improvement of health care systems (34, 35). Undoubtedly, each pharmaceutical that exerted obesity as an undesired effect could be a possible pollutant with obesogenic potential if it is not treated properly. Besides waste, metabolites should be assessed carefully, due to their impact on the environment and as a boomerang-risk to human health.

## Conclusion

The link and, moreover, causality between environmental pollutants and obesity is of high importance, because understanding the relationship between the two can provide valuable insights into the complex factors contributing to the obesity epidemic. Efforts to address the obesity pandemic involve promoting healthy eating habits, increasing physical activity, and implementing policies to create environments that support healthy choices. Furthermore, linking environmental pollution and obesity can highlight the importance of knowledge regarding environmental pollution and preventive measures. Addressing environmental pollution not only has the potential to improve environmental quality, but also to promote public health and prevent obesity-related diseases.

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## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Author contributions

Conceptualization; Ćurčić M, Baralić K, Đukić-Ćosić D; Data curation; Marić Đ, Živanović J, Antonijević Miljaković E, Ćurčić M; Formal analysis; Bulat Z; Buha Đorđević A; Funding acquisition; Antonijević B, Đukić-Ćosić D, Buha Đorđević A. Investigation; Esteban J, Cakmak G, Durgo K, Ćurčić M; Methodology; Esteban J, Cakmak G, Durgo K, Ćurčić M; Project administration; Marić Đ, Baralić K, Antonijević Miljaković E; Resources; Antonijević B, Đukić-Ćosić D Supervision; Esteban J, Cakmak G, Durgo K, Antonijevic B; Validation; Visualization; Baralić K; Roles/Writing – Ćurčić M, Baralić K; and Writing - Esteban J, Cakmak G, Durgo K, Antonijevic B.

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# Zagađivači životne sredine i gojaznost: od uzročno-posledičnih dokaza do otvorenih pitanja

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## Kratak sadržaj

Veza između zagađenja životne sredine i gojaznosti je od velikog značaja, jer razumevanje ovog odnosa može pružiti vredan uvid u složeni set faktora koji doprinose epidemiji gojaznosti. Veruje se da ove hemikalije, zagađujuće supstance, nazvane „obesogeni", ometaju procese metabolizma lipida, čime podstiču razvoj gojaznosti. Antropogene aktivnosti kao što su industrijalizacija, urbanizacija, poljoprivreda i transport značajno su doprinele zagađenju životne sredine. Shodno tome, najznačajniji identifikovani obesogeni su bisfenol A, koji se nalazi u plastici, ambalaži za hranu i termalnom papiru za račune, ftalati, koji se obično koriste u plastici, proizvodima za ličnu negu i ambalaži za hranu, toksični metal(oid)i, pesticidi, koji se koriste u poljoprivredi, kao i perzistentne organske zagađujuće supstance (POPs) i farmaceutski proizvodi (otpad). Rešavanje pitanja zagađenja životne sredine ne samo da ima potencijal da poboljša kvalitet životne sredine, već i da unapredi javno zdravlje i spreči bolesti povezane sa gojaznošću. Rešavanje uzročno-posledične veze između zagađujućih supstanci i gojaznosti moglo bi biti nova i izazovna mapa puta za zdravstvene profesionalce.

**Ključne reči:** gojaznost, plastika, metali, POPs, lekovi (otpad), mapa puta