



## Obesity, Diets and Pollution

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### Editorial

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### Editorial

In the past decades, the problem of obesity has grown exponentially, particularly in the industrialised countries, so that in the next few years the statistical predictions of the World Health Organisation (WHO) estimate that about 20% of the world's population will be obese [1]. At the same time, our knowledge has increased concerning those pathologies associated with obesity, such as cardiovascular diseases [2], diabetes [3-5], arthritic problems [6], cancer [7], chronic kidney diseases [8], etc. In order to try to reduce the negative effects of the obesity, the WHO has implemented a major initiative involving "nutritionists" with the aim of addressing obesity via the alimentary pathway to enable individuals to reach an ideal body weight and help to reduce obesity-associated illness. An extremely large number of diets have already been published; and many of them are routinely in use [9,10].

There is a particular aspect, however, that is underestimated in most of the diets. Indeed, there are usually no indications concerning the possible negative effects of the weight-loss for the health of the patients. Adverse effects may be due to various causes, but one of the most important is that the fat present in the adipose tissue can contain a large amount of the organic lipophilic environmental contaminants accumulated in the body over time. Therefore, as a result of dieting, the liver will receive not only the lipid to be metabolised, but also the toxic environmental chemicals including many persistent organic pollutants (POPs) present in the fat. These pollutant xenobiotics include chemicals such as polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs), polychlorinated dibenzo-p-dioxins and

furans (PCDDs/PCDFs), pesticides etc. If an individual has a weight loss of 4 Kg in a month (a quite usual situation but the decrease can often reach 6-8 kg), the amount of PAHs metabolised in the liver may reach values of 361 µg/kg fat [11,12], dioxin and dioxin like-PCBs 42.7 ng WHO-TEQ/kg fat [13], DDT 420 to 20,000 µg/kg fat [14].

A major function of adipose tissue is the secretion of a wide range of signals and factors termed inflammatory adipokines [15,16], including cytokines (TNF-α, interleukins) and chemokines (MCP-1). Hormones are also secreted by adipose tissue that participate in body weight regulation and glucose and lipid homeostasis (i.e., adiponectin, leptin, resistin) [17]. Reduced adiponectin levels and increased resistin levels with obesity are associated with insulin resistance and inflammation [15,16]. Moreover, mobilisation of lipids and associated lipophilic xenobiotics from adipose tissue during pregnancy may have adverse health consequences for both the mother and developing foetus; and, this may be particularly relevant in pregnancy in obese women [15,18]. Organic lipophilic xenobiotics are metabolised in the liver hepatocytes by enzymes of the cytochrome P450 (CYP) family (Phase I detoxification reactions). These oxidatively biotransformed products are then conjugated by the Phase II enzymes to render them more hydrophilic (for example benzo[a]pyrene, due to its complex metabolism, may be transformed into many compounds such as phenols, diols, triols, quinones, etc [19]). Most of these compounds are finally transported into the bile (Phase III reactions) [20]. From the bile, the xenobiotic metabolites will be transferred into the intestine to be eliminated with the faeces [21]. As for

benzo[a]pyrene, its catabolic products are mainly eliminated with the faeces, with only 0.21% being excreted as 3-OHBP in the urine, as demonstrated in an animal study [22].

This generic description outlined above of the fate of the lipophilic xenobiotic toxic chemicals clearly highlights the risk aspects that need to be considered during dieting:

- It is important to facilitate hepatic functions, as the liver will be subjected to a rather drastic increase in its metabolic activity (i.e., in particular, in relation to enhanced lipid metabolism). In this regard, it should be noted that the physiological functions of the liver can be augmented by using various pharmaceutical products; but it is also possible to use natural nutraceutical product-based occidental and oriental remedies (e.g., plant polyphenolic compounds). Many of these herbal drugs have been used for thousands of years; and some are known to be able to gently support hepatic functions [23].
- The reactive oxygen species (ROS) production associated with the CYP-related xenobiotic metabolism and lipid utilisation may cause oxidative stress in the hepatocytes [24]: a situation that can be, at least in part, avoided through the addition of adequate antioxidants in the diet.
- Bile secretion should be also stimulated to support the rapid transport of the pollutant xenobiotic metabolites from the liver into the intestinal lumen.
- The risk of damage of the intestinal epithelial cells due to the accumulation of toxic substances should also be reduced by increasing the dietary content of natural fibres (both soluble and insoluble). The complex carbohydrates that comprise dietary fibre can bind the metabolites of the xenobiotic compounds and help to promote the intestinal transit of the faeces with more rapid elimination of the toxic (and sometimes genotoxic) chemicals released as a result of the augmented metabolism of lipid deposits in obese individuals [25,26]. Selected dietary fibre components, such as inulin, glucomannan, psyllium etc., are known to have a prebiotic role [27]; and in this way contribute to the development of an effective and healthy intestinal microbiome, a fundamentally important requirement for healthy gut physiology [28].

In addition to their role in carcinogenicity, exposure to PAHs and PCBs are known to increase the risk for cardiovascular disease (CVD), stroke and diabetes [29,30]. Consequently, there may be an additional risk, as a result of weight-loss dieting, for obese patients with pre-existing elevated risk of stroke and diabetes from potential interactive effects of pollutants mobilised from fat depots in obese individuals.

Ironically, when accumulated lipophilic organic pollutants are released from lipid in adipose tissue, this will include endocrine disrupting environmental contaminants that are classed as obesity-inducing obesogens (e.g., bisphenol A, organotins, phthalates, PCBs, dichlorodiphenyl-trichloroethane, and organobromines) [31-33]. Consequently, any release of obesogens from adipose tissue by dieting, may actually exacerbate the obesity problem that dieting is aiming to resolve. This recent evidence confirms the importance of appropriately supporting the patient during the course of the elimination of the toxic metabolites.

It is also important to underline the role of water intake during the diet. Water represents a fundamental constituent for the elimination of the hydrophilic metabolites of pollutant xenobiotics by the kidneys; this physiological process assumes a particular relevance for supposedly therapeutic high protein diets in which it is necessary to eliminate not only the lipid metabolites, but also, an excess of amino acid catabolites resulting from protein breakdown. Usually, consumption of about 2 L/d of water is advised: often, however, no mention of the characteristics of the drinkable water is reported. In this regard, it is necessary to mention that the mineral residue of the drinkable water may vary between 30 mg/L to more than 1000 mg/L [34]. Moreover, the composition of the inorganic components in the water may be qualitatively and quantitatively different in the various kinds of water from disparate geographical locations; and the pH of the water will correspondingly vary. These few indications clearly highlight the importance of selecting drinking water with the right chemical characteristics to help the body to eliminate the xenobiotic derivatives, in relation to the physiological status and characteristics of each patient. In addition, it is important to remember that there are numerous nutraceutical products, most from the field of phytotherapy, that are able to gently augment diuresis and elimination of environmental xenobiotic derivatives [35].

Dietary components are usually considered only in terms of calorific intake and the supposedly appropriate ratios among proteins, carbohydrates and lipids. However, a large body of information concerning whole food in terms of its possible therapeutic roles is now available [36,37]; in particular, the plant nutraceutical components may be viewed, not only in terms of fibre content, but also of the known therapeutic characteristics of a diversity of natural products such as polyphenols that can act as antioxidant and, anti-inflammatory agents, as well as playing a role in regulating the gut microbiota [27,28].

Finally, it should be mentioned that, both the water and food recommended during the diet should be able to shift the pH of the blood towards pH 7.4: this value of pH of the blood (7.35-7.45) is often considered to be the most

natural condition to be achieved by a patient at the end of the nutritional pathway for obesity-related weight loss [38,39].

In conclusion, an important question to pose is: is it practically and ethically appropriate to deploy weight-loss dieting in the obese without adequately taking into account the possible adverse effects that may be caused by the release of xenobiotics from adipose tissue?

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