CHEMICALS AND OBESITY

While diet and exercise are important factors in the obesity epidemic, an emerging body of science demonstrates that exposures to chemical obesogens may be important contributors. A number of chemicals known to disrupt hormones also appear to affect the size and number of fat cells or hormones that regulate appetite and metabolism.

The U.S. is confronting the growing rate of obesity as a major public health problem. One-third of American children, and two-thirds of adults, are obese or overweight.[1] The direct costs of treating obesity alone are $190 billion per year,[2] which might be as high as 16.5 percent of national health care spending.[3] While diet and exercise are widely recognized as important factors in the obesity epidemic, there is an emerging body of science showing that exposures to chemical obesogens may be important contributors. Obesogens are chemical agents that promote fat accumulation and alter feeding behaviors through various mechanisms, and we are all exposed to them every day.

Widespread exposure

Widespread production and use of industrial chemicals in both agriculture and consumer products results in daily exposure to an array of chemicals that build up in the food chain or leach into our food from packaging. We are also exposed to some of these same chemicals from other consumer products and building materials. Hundreds of chemicals are recognized as hormone disrupters that impact the delicate hormone balance in the human body. Hormone disrupters are especially harmful because, like hormones themselves, they can exert health impacts even at minute levels of exposure and exposures in the womb can have lifelong impacts.

Hormone disruption

A number of chemicals known to disrupt hormones also appear to be obesogens.[4,5] A 2011 National Institute of Environmental Health Sciences (NIEHS) expert workshop concluded that the scientific literature supports a link between certain environmental chemicals and increased risk for obesity as well as Type 2 diabetes.[6] Chemicals can affect the size and number of fat cells or the hormones that regulate appetite and metabolism. They can also cause changes in gene expression, or epigenetic changes, which can have intergenerational impacts.[7] Prenatal and early life exposures to chemical obesogens are especially impactful, as they may alter metabolism and development of

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fat cells over a lifetime, as illustrated by the work of Dr. Bruce Blumberg (University of California, Irvine) with organotins (organic compounds containing a carbon to tin bond).

Obesogens old and new

Blumberg first coined the term "obesogens" in 2006, after he discovered the obesogenic effects of tributyltin (TBT), an organotin fungicide still used in wood preservatives and as an additive to polyvinyl chloride.[8] He found that the offspring of pregnant mice fed organotins were heavier than mice that were not exposed. The exposed mice were predisposed to make more and bigger fat cells and in utero exposures caused permanent effects.[9,10] TBT activated a receptor in the body that regulates fat cells known as PPAR or peroxisome proliferator-activated receptor. Chemical "imposters" can bind to the receptor and activate the program that makes fat cells.[11] Chemicals that activate PPAR include tributyltin,[12,13,14] DEHP[15] and its metabolite MEHP.[16,17] While studies of human exposure to TBT are rare, this research provides evidence of mechanisms for obesogenic effects now seen from scores of chemicals to which people are exposed every day.[18]

Some of the chemicals to which humans are exposed on a regular basis are persistent chemicals that accumulate in the food system and in the human body, even though many of them, like DDT, have been phased out of use. There is evidence that DDT exposure is associated with obesity. Exposure to DDT and oxychlordane was associated with increased body mass index and waist circumference.[19] Maternal levels of DDE, a metabolite of DDT, were associated with increase in body mass index (BMI) in adult female offspring.[20] Similarly, in a study of Michigan mothers who consumed fish contaminated with DDT, prenatal DDE levels were statistically and significantly associated with increased weight and BMI of adult offspring.[21] Exposure to DDE was linked to elevated BMI in infancy[22] and in three-year-olds.[23] While DDT has been phased out of use in the U.S., some persistent and bio-accumulative chemicals known to have obesogenic effects are still in use, including brominated flame retardants or PBDEs and perfluorinated chemicals. Other obesogens, including bisphenol A and phthalates, are short lived in the body, but are widely used in food packaging and other products, affording ubiquitous exposures.

EXAMPLES OF CHEMICAL OBESOGENS

Bisphenol A (BPA)

Prenatal and early life exposures to bisphenol A, a chemical commonly used in food packaging, are linked with obesity.

Bisphenol A (BPA) is a chemical component of polycarbonate plastic used in many food and drink containers and in epoxy resins used as coatings in food cans. The Centers for Disease Control (CDC) biomonitoring program has detected BPA in the urine of 93 percent of adults sampled.[24] Scientists have measured BPA in the blood of pregnant women, in umbilical cord blood and in the placenta.[25,26] Exposure levels in one study were comparable to those shown in animal studies to cause adverse effects on reproduction.[27] BPA disrupts hormones in the human body and animal studies show that low-dose early life exposure is linked with reproductive and developmental problems, genetic damage[28] and cancer.[29,30,31] In humans, higher BPA levels in urine were associated with ovarian dysfunction,[32] recurrent miscarriages,[33] cardiovascular diagnoses, diabetes, obesity, abnormal concentrations of liver enzymes[34] and reported heart disease.[35]

There is growing evidence from both animal and human studies of BPA's obesogenic effects. Perinatal and postnatal exposure to BPA in drinking water was associated with increased mean body weight[36,37] and total cholesterol in mice.[38] Exposure of pregnant mice to BPA was associated with insulin resistance in both the mothers and their male pups.[39] Mouse embryos exposed to BPA grew into significantly heavier pups compared with unexposed

BPA is used in metal can linings . CC image courtesy of beana_ cheese via Flickr.

controls.[40] Perinatal exposure to BPA followed by a normal diet resulted in increased body weight, elevated insulin and impaired glucose tolerance in adult rat offspring. In the same study rats

fed a high-fat diet following perinatal exposure to BPA were disposed to severe metabolic syndrome.[41]

Children and adolescents with higher urinary BPA concentrations were more likely to be obese.[42] Higher levels of urinary BPA were linked to higher incidence of diabetes in adults[43] and higher BMI and waist circumference.[44] Exposure to BPA at environmentally relevant doses can inhibit release of a hormone from fat cells that protects humans from metabolic syndrome[45] and is associated with the conversion of connective tissue cells to fat cells.[46]

Regulation in the U.S. as of June 2013:
None at federal level, but 12 states (CA, CT, DE, IL, ME, MD, MA, MN, NY, VT, WA, WI) have banned BPA in baby bottles and cups. VT, CT, MN and ME bans also include baby food and formula containers.

Phthalates

Phthalates are hormone-disrupting chemicals commonly found in plastics and fragranced personal care products."

Phthalates are plasticizers that people are exposed to daily through food, water, air and consumer products. Di-2-ethylhexyl phthalate (DEHP) is of particular concern, as it is a hormone disruptor and a possible human carcinogen, affecting the liver.[47,48] Exposure is associated with liver and thyroid toxicity, reproductive abnormalities and adverse effects on the respiratory system, including asthma.[49] The CDC biomonitoring program has identified metabolites of DEHP in nearly everyone tested.

There is evidence that DEHP, a phthalate used in PVC, is an obesogen. Higher urinary phthalate metabolite concentrations in adult males were associated with increase waist circumference and insulin resistance.[50] Similarly, urinary concentrations of some phthalate metabolites were associated with higher BMI and waist circumference for adults.[51] Children with higher DEHP levels were more likely to have higher body mass index.[52] The phthalate MEHP activates metabolic sensors that regulate fat cells,[53] similar to effects seen with organotins.

Some children's shampoos contain phthalates. CC image courtesy of thejbird via Flickr.

Regulation in the U.S. as of June 2013:
Federal law bans some phthalates in toys and baby products and preempts state laws regulating phthalates in these products.

PBDEs (polybrominated diphenyl ethers)

Evidence of potential obesogenic effects from exposure to PBDE flame retardants is growing.

PBDEs (polybrominated diphenyl ethers) are chemical flame retardants used in foam products, textiles, electrical equipment, building materials and transportation. PBDEs are persistent in the environment and bio accumulate in animals and humans. CDC biomonitoring studies find PBDEs in everyone tested. Animal studies confirm that PBDEs are toxic to developing organisms, with adverse effects on the brain, reproductive system and liver. They also disrupt thyroid function.[54,55] Because PBDEs accumulate in fatty tissue, dietary intake of animal-based foods contributes to high body burdens of PBDEs in the U.S.[56] Children have higher levels of these chemicals in their bodies due to both dietary exposure and exposure through household dust.[57,58]

Polyurethane foam used in furniture may contain PBDEs. CC image courtesy of Tom & Katrien via Flickr.

Evidence from both animal and human research points to PBDEs as potential obesogens. Rats exposed to PBDEs experienced altered insulin and metabolic changes[59] and increased body weight.[60] American kestrel nestlings exposed to PBDEs had increased body weight.[61] Higher body mass index was correlated with higher levels of PBDEs in human breast milk[62] and in placental tissue.[63]

Regulation in the U.S. as of June 2013:

None at federal level. Eleven states have banned the use of octa and penta-BDE and four states ban some uses of deca-BDE (ME, WA, VT, OR). Companies that make penta and octa voluntarily phased them out in 2006 and makers of deca- BDE phased it out in 2009.

Perfluoroalkyls, notably PFOA or perfluorooctanoic acid

Perfluoroalkyls, notably PFOA or perfluorooctanoic acid is one of the persistent perfluorinated chemicals (PFCs) used in a variety of industrial and consumer product applications, including Teflon coated cookware and grease resistant food packaging coatings e.g., pizza boxes, fast food wrappers and popcorn bags.

Environmental contamination of drinking water and fish exposes communities in the vicinity of manufacturing sites. Global transport of PFCs and subsequent accumulation in the food chain expose fish and meat eating populations as far north as the Arctic. CDC biomonitoring studies have found four PFCs in nearly everyone tested.[64]

Studies of laboratory animals and wildlife provide evidence of reproductive, developmental, and systemic health effects. Higher levels of PFOA (and perfluorooctane sulfonate, PFOS) in blood were associated with increased risk of infertility,[65] reduced semen quality in men,[66] and thyroid disease in adults.[67] More research is needed but there is some evidence that PFCs are associated with risk factors for obesity. Low birth weight is a risk factor for obesity later in life. Mice exposed to PFOA in utero had lower birth weight, reduced survival and developmental delays.[68] There is evidence from cross-sectional studies that human exposure to PFOS and PFOA is associated with reduced birth weight,[69,70] but whether this is linked to later development of obesity is still unknown. In utero low-dose exposure of mice to PFOA was associated with significant increase in body weight and serum insulin at midlife, while there was no effect on body weight from adult exposure,[71] illustrating the importance of critical developmental windows in the occurrence of obesity.

Some non-stick cookware contains PFOA. CC image courtesy of JPC24M via Flickr.

Regulation in the U.S. as of June 2013:

None. 3M company stopped making these chemicals in 2002.

Other obesogens

Other obesogens include cigarette smoke, antipsychotic drugs and some other pharmaceuticals, fructose, genistein, monosodium glutamate (MSG), other organochlorine pesticides (in addition to DDT), PCBs, lead, benzo[a]pyrene, diesel exhaust and fine particulate matter.[72,73]

Obesogens in common consumer products

Chemical name	Products found in
Bisphenol A (BPA)	Polycarbonate plastic, food can linings, baby food jar lids, dental sealants, thermal credit card receipts
Phthalates (e.g., DEHP)	Softners in PVC plastic, fragrance-binder in personal care and cleaning products, food packaging
Polybrominated diphenyl ethers (PBDEs)	Flame retardants in electronics, textiles and polyurethane foam
Perfluoroalkyls (e.g., PFOS & PFOA)	Teflon-coated cookware, grease-resistant food packaging (fast food wrappings, pizza boxes, microwave popcorn bags)

Conclusions and recommendations

Obesogenic chemicals like phthalates, bisphenol A, PBDEs and perfluorinated chemicals are ubiquitous in the human environment. The fact that CDC biomonitoring studies have found all of these chemical in nearly everyone tested provides evidence of widespread exposure. Like other hormone disrupting chemicals, early life exposures to obesogens can cause subtle adverse effects even at low doses. While fat accumulation is impacted by the quality and quantity of the food we eat and how many calories burned through activity, it is also governed by complex metabolic processes that regulate appetite, metabolic rate, glucose levels and the number, size and metabolic activity of fat cells. It is now evident that a variety of environmental chemicals can act on cellular pathways to promote fat accumulation and obesity.

In light of a growing obesity epidemic in the U.S., actions to protect public health by preventing exposures to obesogenic chemicals should be undertaken, including:

1. Better regulation of toxic chemicals through reform of the Toxic Substances Control Act (TSCA). TSCA should be strengthened to require the phase out persistent, toxic bio-accumulative chemicals that build up in the food system and in the human body and to require basic safety testing on all new chemicals introduced into commerce. See saferchemicals.org and healthylegacy.org.

2. State and federal regulations to prevent food contact uses of chemical obesogens, such as BPA and phthalates to prevent routine exposure.

3. Investment in green chemistry research and public policies that incentivize and support businesses in using green chemistry innovation to develop safer chemicals and safer products. See greenchemistrymn.org.

4. Voluntary efforts by leading downstream businesses and retailers to phase out the worst chemicals. See mindthestore.org

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