Endocrine disruption and fat-causing “obesogen” theories crumbling as research rolls in

Most scientists, physicians and the public suspect two culprits behind obesity — diet and exercise. But several other possible causes have popped up. Genes, stress, sleep, gut microbiomes and medications all seem to be fair game for causing our increased fatness. Yet another category — obesogens — has become the darling of environmentalists, natural food advocates and others in search of an industrial cause of obesity.

The term obesogen was coined by University of California Irvine scientist Bruce Blumberg in 2006, when he and colleagues reported on the possibility that chemicals in our environment — in his case, tributyltin, which was used in coating the hulls of boats and ships — could disrupt metabolism via our endocrine system, leading to excess fat tissues in our bodies. The research — very speculative and in its early stages — fit well with a belief, widely embraced by anti-chemical NGOs but also by some toxicologists, that environmental chemicals played a major, if obtuse, role in a range of maladies, including obesity.

Almost immediately after the phrase was coined, advocacy groups and politicians scrambled to push for bans on various chemicals believed to be ‘endocrine disrupting’ obesogens. The Natural Resources Defense Council in 2008 petitioned for a ban on the chemical Bisphenol A (BPA), used in a wide array of plastic manufacturing, as a suspected “endocrine disruptor” that “has been associated with a wide range of adverse effects, including reproductive defects, chromosomal damage, nervous system harm, increased rates of breast and prostate cancer, and metabolic changes including obesity and insulin resistance.” More recently, the NRDC has stated its support of the U.S. Consumer Products Safety Commission ban on another alleged “endocrine disruptor,” the phthalate class of plasticizing chemicals.

On Capitol Hill, several bills over the years have proposed to ban BPA and other ‘environmentally dangerous’ chemicals, even though (in the case of BPA), the FDA has repeatedly determined that the chemical was safe, and that these chemicals have been widely used for decades before obesity rates began rising. Pressured by activists, the European Food Safety Authority — which operates under the Precautionary Principle that has led to numerous restrictions on controversial chemicals — last year reviewed the claims about dietary exposure of BPA and found “no consumer health risk from bisphenol-A exposure,” rejecting the obesity fears, among other claims.

While science was coalescing around the evidence that obsegons was more fear than susbstance, the movement gained momentum, when hucksters like Dr. Mehmet Oz warned of a “new group of secret saboteurs in the war against weight gain.”

> Chemicals we’re exposed to everyday could be a big part of the obesity epidemic. Called obesogens, or endocrine disruptors, these natural and man-made chemicals work by altering the regulatory system that controls your weight — increasing the fat cells you have, decreasing the calories you burn, and even altering the way your body manages hunger.

What's really going on? Are there chemicals that we've been exposed to that could cause obesity? Is there a thing called an endocrine disruptor?

Disruptive cause that plays second fiddle

No scientist has said that chemicals in our environment are more responsible than caloric intake and caloric output for obesity. However, these chemicals have been introduced as a possible "third way" that we've been getting bigger.

Much of the science behind these "endocrine disruptors," is problematic. And even though nearly all scientific studies have adopted the term, careful studies have shown that that description is a gross over simplification.

The human endocrine system is very complex. Its various pathways include the molecules estrogen, testosterone, catecholamines, thyroid hormones, steroids, growth hormones, insulin, leptin, and others. All of these molecules operate through a network of receptors, which can be inhibited or stimulated by their matching hormones and other molecules, or other chemicals. The idea behind "endocrine disruptors" was that somehow man-made chemicals such as BPA, phthalates, PCBs or pesticides could alter how these molecules and their networks normally function. But, as a recent paper on "obesogens" warned, using the approach of analyzing individual participants in these networks has problems:

> (the approaches) Are limited because they cannot accommodate redundant pathways, they do not accurately represent multifarious interactions with a variety of receptors in different tissues, nor do they account for effects that require time to present.

So far, research on the role of BPA, phthalates, pesticides and others on obesity has been focused on in vitro studies, or in laboratory rats. The human studies so far have been largely epidemiological, finding correlations (often described as "links" or "associations" in scientific and popular media). A 2014 study on the possibility that phthalates are obesogens reviewed 26 epidemiological studies that showed no firm pattern. The study authors concluded:

> We found no inter- or intra-study consistency for any phthalate metabolite for any of the indicators of overweight/obesity, DM or CVD in children or adults. Most reported associations were not statistically significantly different from the null, some were positive, and others were inverse.

Rigorous prospective studies which could identify the mechanism of this chemical alteration leading to obesity have been rare, and have shown some opposite effects:

- A 2009 study by U.S. Environmental Protection Agency scientists showed that newborn rats did not have any changes in puberty, development or behavior after exposure to Bisphenol A (BPA). However, exposure to the birth control pill ingredient estradiol did result in changes to newborn rats.

- Last June, researchers at North Carolina State University found that BPA had no independent effects of weight change or feeding behavior with pregnant rats and their offspring. However soy, which naturally 'disrupts' endocrine levels. did result in weight gain on the newborn (offspring) rats.

If soy and birth control pills could be endocrine disrupting obesogens, then why not ban them, too? If dose-response curves show little to no effect of these chemicals, then what's wrong with them?

One tactic that's being used to justify the bans on BPA is the so-called "U shaped dosage curve," or "Homesis." This idea claims that very low dosages of a pesticide or other chemical could elicit a toxic response, but increasing dosages would actually show decreases in response, followed by toxicity responses in very high dosages. This idea is by no means accepted by scientists. Richard Sharpe, a scientist at the Center for Reproductive Biology at the Queen's Medical Research Institute in Edinburgh, observed that such dosage curves meant that "a ligand, such as Bisphenol A, activated wo separate pathways with differing threshold sensitivities, but which impinge on a similar downstream pathway." And finding exactly what those pathways are would require much more than epidemiology.

Another defense of obesogens and endocrine disruptors lie in the new field of epigenetics. Such events, such as DNA methylation or alteration of histones, could affect how a gene is regulated without changing the nature of the gene itself. In addition, many scientists have been experimenting with the possibility that events, such as exposure to obesogenic chemicals, could be carried on via these epigenetic mechanisms to further generations. However, the complexity of the "epigenome" is even less well known that all the mechanisms that could lead to obesity, and, as a UCLA team pointed out, many of these epigenetic actions are reversible.

Washington to the rescue?

The US Government might just be able to put an end to the controversy with some real science. The EPA has always had authority to test toxic chemicals under the Toxic Substances Control Act (TSCA), but has tested only 200 of the 60,000 on its list of potential chemical hazards. And its endocrine disruptor testing program showed 32 chemicals with some endocrine activity, 14 of which were ruled safe. To speed up this testing regimen, a new high-throughput program called ToxCast was initiated by the agency, which promises more comprehensive scientific reviews to determine the safety of these chemicals.

Two of those chemicals that may pass the safety test? BPA and phthalates, which were removed from an EPA list of "chemicals of concern" recently. Real science on these chemicals in particular and the concept of how the endocrine system responds to the environment would be welcome.

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