Prevention®

What's Really Behind The Rise In Obesity

What's Making America So Fat?

It may not just be due to too much food and too little exercise—some experts suspect environmental chemicals could also be to blame

By Robin Marantz Henig

Of all the modern trends that have been linked to America's ever-expanding waistline—portion size, more McDonald's, couch potato lifestyles, and some lesser-known possibilities, like air-conditioning, viral exposure, and lack of sleep—one of the weirdest is designer handbags.

If your brand-name clutch is making you fat, it would be because it contains, as at least some high-end handbags do, a new kind of chemical to worry about: compounds known as obesogens.

Obesogens are believed to work in at least three ways: first, by directly affecting adipocytes, or fat cells, by either increasing their fat-storage capacity or increasing their number; second, by changing metabolism, by both reducing the number of calories burned at rest and promoting the storage of calories as fat; and third, by changing the way the body regulates feelings of hunger and fullness.

Don't think you're avoiding them because you've never paid a week's salary for a purse. Obesogens are ubiquitous. If you've ever eaten seafood, plugged in an air freshener, handled a cash register receipt, eaten canned vegetables, sat on a couch treated with flame retardant, or cooked in a nonstick pan, you've already been exposed. (Taking showers with vinyl curtains count, too.) Most alarming is new animal research that suggests that chemicals to which your parents, grandparents, or great-grandparents were exposed—including the long-banned pesticide DDT—can cause you to gain weight, even if you've never been exposed yourself.

"It's impossible to know the precise contribution of obesogens to the obesity epidemic, but I

would bet that it's significant," says Bruce Blumberg, PhD, professor of developmental and cell biology at the University of California, Irvine. Even on a normal diet, he says, mice in his lab that are exposed to obesogens in utero grow up to be about 15% heavier than unexposed mice. "Fifteen percent," he says. "That's the difference between what we weighed a generation ago and where we are now."

Of mice and men

The obesogen hypothesis was unknown back in 2005, when Dr. Blumberg submitted his first grant application to study it. Some reviewers were outraged, he says. "How dare you waste our time with such a ridiculous idea?" one wrote. That grant was rejected, no surprise, but by 2007, Dr. Blumberg and a handful of other researchers managed to get the funding they needed to explore the connection between toxins in the environment and the global obesity epidemic.

When Dr. Blumberg and his colleague Felix Grun, PhD, used the term obesogen for the first time in 2007, they applied it to a variety of chemicals, including tributyltin (TBT), a fungicide that can contaminate seafood and drinking water. (The usual route: via TBT-treated boat hulls, docks, and fishing nets, where it was once used to discourage barnacle encrustation, as well as industrial water-cooling systems used in paper, leather, and textile mills, which discharge wastewater into rivers and streams.) They fed pregnant mice a single dose and found that the offspring were born with greater fat stores than normal. At 10 weeks of age, these mice weighed about 15% more than mice that had not been exposed to TBT before birth.

More from Prevention: 6 Most Toxic Things In Your Purse

Even more worrisome was the trend that Dr. Blumberg and his colleagues found when they followed prenatally exposed mice through subsequent generations. The mice born to the second generation of fatter mice (that is, the mice who had been exposed in utero) were also fatter—even though they'd had no direct prenatal exposure to TBT.

There's a simple explanation, Dr. Blumberg says: "If you expose a pregnant female, inside the fetuses are germ cells [immature sex cells] that will be the grandchildren." In other words, altered egg cells in the second generation can be expected to give rise to fatter mice in the third generation. But here was the surprise: When the fatter third-generation mice had pups, the pups were also fatter—even though this fourth generation was never exposed to chemicals, not even indirectly through their mothers.

"Once it's in the great-grandchildren, it's permanent," Dr. Blumberg says. The effects, known as epigenetic changes, can be passed along from one generation to the next, long after the original exposure has passed.

Recently, reproductive biologist Michael Skinner, PhD, and his colleagues at Washington State University reported similar dire news about another obesogen, DDT. The pesticide has been banned in the United States since 1972 but can still be found—in the form of a by-product, DDE—in the urine of pregnant women in many parts of the country. In Dr. Skinner's study, female rats exposed prenatally to DDT did not grow up to be obese, but 50% of their great-grandchildren did—even though they had no direct DDT exposure. Dr. Skinner's bottom line: "Obesity may be in part due to environmentally induced epigenetic transgenerational inheritance."

If the effects of obesogens really can last long after exposure, then identifying and eliminating them takes on a special urgency. While DDT isn't used in the United States, TBT still is. Though it's no longer mixed into marine paints because of a global ban, TBT is still permitted in a variety of common household products, such as wood preservatives; disinfectants; and tiles, shower curtains, and window blinds made with polyvinyl chloride. It also persists in the food chain. If what occurs in lab animals holds true for humans, this chemical could be contaminating generations to come.

Hormonal havoc

Most obesogens are classified as endocrine disruptors, a category made famous by recent controversies regarding BPA (bisphenol A) in baby bottles and canned food. Endocrine disruptors interfere with the action of a variety of hormones, especially estrogen and testosterone, and have been associated with problems in the reproductive, neurological, and immune systems, as well as cognitive development. Though the FDA has taken steps toward eliminating BPA from pacifiers and sippy cups, it's still ubiquitous, found in everything from medical devices such as catheters and IV equipment to cash register receipts and the inside of metal food cans. It's also in your home's water supply pipes if they're made of polyvinyl chloride (PVC). The CDC estimates that 92.6% of Americans age 6 and over have some BPA in their urine.

Dose matters, but in a surprising way. Unpublished research from the University of Missouri suggests that BPA is actually more potent at very low doses—1,000 times below the level thought to be safe—than at high doses. This is probably related to a phenomenon known as

receptor down regulation. Hormone receptors usually respond to very low levels of hormone, so when a compound like BPA mimics a hormone, it, too, can spark a response at a very low dose. At these very low levels, an endocrine disruptor can fool the body into creating more hormone—and, in the case of BPA, more fat cells.

Obesogens are probably most dangerous when fat cells are forming most rapidly: during the critical window of fetal and early development. That's what makes soy infant formula—which, according to the American Academy of Pediatrics, may account for nearly 25% of the infant formula market—so worrisome. It contains genistein, a chemical that naturally occurs in soy. Genistein is an endocrine disruptor linked to obesity in experimental animals.

Retha Newbold, a now-retired federal biologist, studied the obesogenic effect of genistein in newborn rats. She gave a group of them a dose of genistein comparable to what a human infant would get on an exclusive soy-formula diet. When she looked at the rats again at 3 or 4 months of age, those that had been fed genistein as newborns had more fat stores and higher weights than the control group, even though there was no difference between how much the two groups were eating or exercising.

Some endocrine disruptors can work to cause weight gain through a mechanism known as the PPAR gamma pathway. PPAR gamma (short for peroxisome proliferator-activated receptor gamma) is expressed in cells called preadipocytes (pre–fat cells) and becomes set in the "on" position, which stimulates preadipocytes to become adipocytes, thereby increasing the number of fat cells in the body.

Phthalates are another class of chemicals that are also more likely to increase the risk of obesity in people who were exposed prenatally. Dibutyl phthalate, for instance, has been shown to cause developmental disorders in male offspring exposed in utero, and di(2-ethylhexyl) phthalate has been linked to thyroid irregularities that could affect metabolism. Phthalates are found in the artificial fragrances used in personal-care products such as shampoos and body lotions, as well as in air fresheners, scented candles, and nail polish.

Sunscreens, shampoos, detergents, pajamas—the list of products that might contain obesogens is long. Even the healthiest-seeming items on the list can be suspect: Leafy vegetables, for instance, are often treated with triflumizole, a fungicide that has been shown to cause obesity in mice. Pregnant women might be passing obesogens to their offspring by exposure to

contaminants that are so commonplace, they're hard to avoid.

Scientists at the University of Albany detected possible obesogens in a variety of household products: wallpaper, tile, vacuum cleaner dust, and a designer handbag (the researchers didn't specify the designer). And the nonstick cookware touted as healthy because it lets people cook without adding butter or oil is made with another possible obesogen, perfluorooctanoic acid, also known as Teflon. PFOA is used not only in pots and pans but also in lots of housewares with proof in their descriptions—stainproof carpets, greaseproof food wrappers, waterproof clothing.

In another odd twist, the hand sanitizers used by some people because they're so careful about their health contain triclosan, which is also a possible obesogen. One way triclosan may affect body weight is by interfering with thyroid hormone, which regulates metabolism. (Try this DIY recipe for sanitizer you can trust.)

According to R. Thomas Zoeller, PhD, a professor of biology at the University of Massachusetts, Amherst, if the presence of triclosan leads to impaired thyroid function, metabolism could slow, causing weight gain. Dr. Zoeller suggests reducing the spread of colds and flu simply by washing your hands with soap—plain soap, not antibacterial types, which can also contain triclosan. (Here's how to get antibacterial soaps and triclosan out of your life.)

Humans getting heavy

Obesogens can have an impact on adults as well. As Dr. Blumberg points out, certain medications, such as the diabetes drug Avandia, are notorious for causing weight gain. Phthalates have been shown to have an effect on adults, too: A 2007 study at the University of Rochester found that phthalate by-products in the urine were associated with bigger waistlines and increased insulin resistance in men.

Those who are already overweight might be especially susceptible. In 2013, a team of scientists at Inserm—the French version of the NIH—fed a group of mice a high-fat diet containing low doses of some putative obesogens: dioxins, PCBs (found in vinyl tiles and purses), phthalates, and BPA. Most of the mice, both male and female, experienced metabolic changes, but the females developed worse glucose control and had extra trouble: alterations in the estrogen pathway. When working normally, this pathway can offer some protection from metabolic syndrome, a cluster of conditions—excess belly fat, high blood pressure, high cholesterol, and elevated glucose—that are the reason obesity is a health risk, explain researchers Brigitte Le

Magueresse and Danielle Naville.

Animal experiments are great, as far as they go. They've helped scientists discover a connection between chemicals and weight gain and work out the possible mechanisms for how it might work. But that's not quite enough for those who resist the idea that obesogens exist, such as the food and chemical industries whose products are implicated. What are needed still are studies involving humans.

Those are, obviously, much trickier to do. You can't just feed one group of newborns an obesogen and use another group as a control to see what happens when they grow up. The best you can hope for in humans is what Robert Lustig, MD, a professor of pediatrics at the University of California, San Francisco, calls causal medical inference—the most convincing kind of evidence available, short of a controlled clinical trial, which no one can ethically do in the case of obesogens.

Causal medical inference comes from population studies that have found a connection between obesogen exposure and body weight. One such study, conducted at New York University in 2012, looked at BPA levels in more than 2,800 young people ages 6 to 19. Among those with the highest urinary levels of BPA, 22% were obese; among those with the lowest levels, only 10% were. The obesity rate for most Americans in that age range is about 18%.

That's a dramatic association, but lead author Leonardo Trasande, MD, points out that it's still hard to distinguish cause and effect. It could be that people with high BPA levels have an increased tendency to gain weight—or it could be that people who are already fat have higher levels of BPA in their urine, because the chemical is stored in fat cells. Dr. Trasande thinks that the evidence points to the first explanation. "Laboratory and animal studies add plausibility to the notion that BPA may be an obesogen," he says.

And human evidence continues to mount. For one thing, newborns are bigger than ever. "If you look at birth weight around the world, it's been going up a lot: 200 g per baby over the past 25 years," says Dr. Lustig. That's a little less than 1 pound heavier, which almost sounds positive—perhaps a sign of better nutrition in pregnant women worldwide. But Dr. Lustig insists that it isn't a good thing; it's a problem. When newborns are submitted to a DEXA scan—a two-beam x-ray that measures body composition—that 200 g turns out to be "all fat," he says. "These babies are laying down more fat cells even before they are born. And once you make a fat cell, it

wants to get filled." In Dr. Lustig's view, these bigger, fatter babies are more likely to struggle with weight their entire adult lives.

When a trend toward higher birth weight occurs across populations, he adds, it's a good bet something is crossing the placenta. And it must be an all-purpose, widely dispersed something, because it occurs all over the world, and not only in human babies but in lab animals, too.

This is an especially puzzling fact, since laboratory animals' diets and activity levels have remained constant over the past 20 years. But during that time, every species of lab animal that has been weighed and measured—marmosets, macaques, chimpanzees, vervet monkeys, rats, mice—has shown an increase in body weight, from 7.7% to 35% per decade, depending on the species. Since the calories-in/calories-out balance hasn't changed for these animals, something else must be going on.

So, what now?

New York Times columnist Nicholas Kristof has called obesogens the tobacco of our time, a danger to public health about which scientific evidence keeps accumulating while politicians do nothing. "Science-based decisions to improve public health, like the removal of lead from gasoline, have been among our government's most beneficial public-policy moves," Kristof wrote early last year. He suggested that a "starting point" would be to fund more research into the relationship between environmental toxins and human obesity.

Slowly, politicians are starting to pay attention. The White House Task Force on Childhood Obesity mentioned obesogens in its 2010 report to President Obama, suggesting that "fetal and infant exposure to such chemicals may result in more weight gain per food consumed and also possibly less weight loss per amount of energy expended...[which might] persist throughout life, long after the exposures occur." The task force recommended more research and was followed by a 3-year effort launched in 2011 by the National Institutes of Health to investigate the role of chemical toxins in the development of obesity, diabetes, and metabolic syndrome.

If nothing else, the obesogen hypothesis should force people to reconsider the prevailing view of how people get fat. The so-called energy balance hypothesis might be undermined as evidence piles up about obesogens, wrote Dr. Blumberg and his grad student, Amanda Janesick, in a chapter they contributed to Dr. Lustig's recently edited volume *Obesity before Birth*. As scientists learn how obesogens affect metabolism, fat cell number and function, and hunger signaling,

they wrote, they might ultimately move beyond "the simplistic model that caloric intake and exercise can be trivially balanced like a checkbook to achieve optimum weight."

So if obesogens really do contribute to weight gain, who should make a real effort to avoid them? Everyone, says Dr. Blumberg, "but the people who need to be most careful are women who may become pregnant, are pregnant, or have young children. I think that's the most vulnerable group."

That means women of childbearing age should try to purge chemicals from their households as much as possible, opting for organic fruits and vegetables; buying cosmetics that do not contain endocrine disruptors; avoiding canned, prepackaged, and processed foods; and removing plastics from their lives as much as possible. And consider putting away that gorgeous designer satchel until after the kids are grown.

More from Prevention: 70 Simple Ways To Go Green

Published December 2013, Prevention | Updated December 2013

http://www.prevention.com/health/healthy-living/whats-really-behind-rise-obesity