

What Do We Know about Obesogens? with Bruce Blumberg

Ashley Ahearn

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Human beings, as a species, are putting on weight. Obesity rates are rising in rich and poor countries alike for a variety of reasons, from changing dietary habits and activity levels to exposure to artificial nighttime light. Mounting evidence from over the past decade suggests that certain chemicals may be playing a role as well. For some people, so-called obesogens may be altering their metabolism and fat cell development, making it harder to maintain a healthy weight. In this podcast, host Ashley Ahearn talks with Bruce Blumberg about the state of our understanding of obesogens.

AHEARN: It's *The Researcher's Perspective*. I'm Ashley Ahearn.

Human beings, as a species, are putting on weight.

Obesity rates are rising in rich and poor countries alike. And research shows there are many potential causes for this trend, from changing dietary habits and activity levels to exposure to artificial nighttime light.

Mounting evidence from over the past decade suggests that certain chemicals may be playing a role as well. For some people, so-called obesogens may be altering their metabolism and fat cell development, making it harder to maintain a healthy weight.

Dr. Bruce Blumberg coined the phrase "obesogen" in 2006. He's a professor of developmental and cell biology at the University of California, Irvine, and joins me now.

Hi, Dr. Blumberg.

BLUMBERG: Hi, Ashley.

AHEARN: Dr. Blumberg, what turned you on to obesogens? Tell me about your experiments with organotins and lab mice.

BLUMBERG: We were testing organotinsⁱ for their ability to activate a different receptor that we work on called the steroid and xenobiotic receptor as a part of a group of chemicals in collaboration with a laboratory in Japan to test whether these chemicals might be metabolized differently in different species. And at the same time I happened to hear at a meeting in Japan that tributyltinⁱⁱ could sex-reverse fishes, so I said, "That's interesting. Guys in the lab, let's test whether tributyltin activates other hormone receptors as well." And we found that it activated a receptor called PPAR-gamma, which is the master regulator of fat cell development.

That led us to test the ability of tributyltin to cause cells in culture to become fat cells, and we tested the effects on mice and found out that it could make mice fat also.

AHEARN: So, these obesogens are often endocrine-disrupting chemicals as well. What are the similarities there?

BLUMBERG: Well, so the majority of obesogens are endocrine-disrupting chemicals, and the reason that is, is because endocrine-disrupting chemicals typically work on hormone receptors, and many obesogens do the same.

AHEARN: So, what was going on in the mice? What's the mechanism here?

BLUMBERG: Well, the mechanism is that PPAR-gamma, activation of PPAR-gamma, causes there to be more and larger fat cells in these animals and predisposes a type of stem cell in the animals called a mesenchymal stem cell to want to become a fat cell.

AHEARN: Ok, so you're seeing it in mice—how do you make the jump to the human population? Can we extrapolate?

BLUMBERG: Oh, that's an easy one. So, there are pharmaceutical drugs that activate the same receptor—called Actos and Avandiaⁱⁱⁱ—that are known to make people fat. So that experiment's actually been done. So if I give humans a drug that activates PPAR-gamma, and they get fat, why would you imagine that a chemical that activates the same receptor wouldn't have exactly the same effect?

AHEARN: How many other chemicals like this are we exposed to in our daily lives? What are the main obesogens that you watch and you would say are concerning?

BLUMBERG: Well, right now there's a list of about 20 known obesogens, but that's just because the field is relatively young. So organotins are certainly one class for which we know a lot about. Bisphenol A and its relatives are another class—so, for example, bisphenol A is a well-known obesogen, based on the work of Ana Soto and Beverly Rubin^{iv} and Fred vom Saal,^v and we recently published in *EHP* that a related chemical called BADGE—bisphenol A diglycidyl ether—is a very potent obesogen in stem cells and in preadipocytes.^{vi}

Perfluorooctanoic acid (PFOA) and its relatives are relatively well-known obesogens.⁴ There's some evidence for phthalates, and there's varying levels of evidence for other chemicals.⁴

AHEARN: So I'm hearing this list, and I'm thinking, phthalates, bisphenol A—these are chemicals that show up in 95% of the population, according to the CDC.^{vii}

BLUMBERG: That's correct.

AHEARN: So what does that make you think when you look at the average member of the American population?

BLUMBERG: Well, certainly that chemical exposure has the potential to influence almost all, if not all Americans.

AHEARN: So how much of the rise in obesity that we're seeing in the population in the U.S. do you think could be attributed to obesogens?

BLUMBERG: Oh, that's utterly impossible to say without knowing to what extent we're all exposed. So, we know a fair bit about bisphenol A exposure, but we don't know about exposure to almost every other obesogen. We know nothing about organotin exposure. We know almost nothing about PFOA exposure. We know relatively little about exposure to the other obesogens that we're working on. So without knowing the extent to which people are exposed and whether there's a link between the presence of these chemicals and obesity, it would be premature to say that obesogen exposure is responsible for X percent of obesity.

AHEARN: At what point in our lives are we most vulnerable to obesogen exposure?

BLUMBERG: That's also a good question. So, the data from Actos and Avandia say that people can become fat as a result of obesogen exposure at any time of their life.^{viii,ix} I personally believe that it's the early-life exposure that's going to be most important because that's the time when the number of fat cells is being programmed and when metabolic setpoints^x are being established. So I would say from the prenatal period until about the end of puberty is the time we need to be most concerned about.

AHEARN: So, I've got a devil's advocate question here for you: One might see obesogens as the perfect excuse to just give up on weight loss. I mean, if my chemical exposure is making it hard for me to lose weight, and if I'm exposed to these chemicals all over the place—why bother?

BLUMBERG: Well, because I think it's important to note that whether you're exposed or not to obesogens doesn't determine whether or not you'll be fat. I think that if you're the type of person who struggles with weight loss you might say, "Well, I've been exposed to these chemicals, and it's adjusted my metabolism to make me more efficient at storing fat. Therefore, I have to try a little harder, and that's just the way it is," rather than saying "Aw, the hell with it. I'll never succeed." And it could explain why some people fight a lifelong battle against gaining weight.

The statistics show that people who work very hard and who lose a lot of weight, even hundreds of pounds, that 90 percent of them will gain it back,^{xi} and the typical medical explanation is that "well, you just went back to your old bad behaviors." But maybe there's more to it than that. Maybe we're dealing with metabolic set points

here that have to be accounted for and have to be incorporated into a long-term weight-loss plan.

AHEARN: Dr. Blumberg, I realize you're not a dietician or a medical doctor, but what would you say, what do you do in your own life to work your knowledge of obesogens into the way you manage your own weight, or what would you say to other folks that are concerned about their exposure to obesogens?

BLUMBERG: I would include obesogens as part of a larger group of endocrine-disrupting chemicals, and I think it's probably wise and beneficial at any stage of your life to minimize exposure to such chemicals. So in my house we eat organic food as much as possible. We minimize plastic in our lives. We minimize the amount of processed food that we eat. We don't eat a lot of canned and prepackaged foods. My wife is very fond of cooking fresh food. We avoid too much added sugar, which if you make the food yourself you don't have to worry about what's in there or where it came from, right? You have some control over that. So I think these are all things that we can do in our own lives to minimize exposure to endocrine-disrupting chemicals, and I think that has a long-term benefit.

AHEARN: Do you think there will ever come a time when our diet smoothies will say "this product is obesogen-free"?

BLUMBERG: That would be interesting. Do I think that will ever happen? Hmm. I'd be surprised, but I'd never say never.

AHEARN: How do you hope your research is used in making decisions like labeling products or policy decisions?

BLUMBERG: That's a difficult question. It's not my job to help to establish policy or things like that. It's my job to do the best research that I can that really addresses questions and answer them clearly such that those data are available to the people whose job it is to make policy.

AHEARN: Ok, so which questions are you looking to answer and do you feel most necessary to answer in the near future on this subject?

BLUMBERG: So, for us we're most interested in the details of the molecular mechanisms of how obesogens act, and we have a couple that we're working on. We're interested in the potential for long-term and transgenerational effects. So, do the effects of obesogen exposure early in life persist in our children, our grandchildren, and our great-grandchildren, as has been shown for some endocrine disruptors? For me those are the questions that I find most exciting.

AHEARN: Dr. Blumberg, thanks so much for joining me.

BLUMBERG: You're welcome.

AHEARN: Dr. Bruce Blumberg is a professor of developmental and cell biology at the University of California, Irvine.

And that's *The Researcher's Perspective*. I'm Ashley Ahearn. Thanks for downloading!

Ashley Ahearn, host of *The Researcher's Perspective*, has been a producer and reporter for National Public Radio and an Annenberg Fellow at the University of Southern California specializing in science journalism.

References and Notes

ⁱ Organotins are chemical compounds that include tin and carbon. These compounds are used as biocides, heat stabilizers, and catalysts in a variety of industrial and agricultural applications.

ⁱⁱ Tributyltins are a type of organotin whose biocidal properties are utilized in applications such as wood preservatives and antifouling paint to keep the hulls of boats and ships clean of marine organisms.

ⁱⁱⁱ Actos (pioglitazone) and Avandia (rosiglitazone) are used in conjunction with diet and exercise to control type 2 diabetes.

^{iv} Rubin BS. Bisphenol A: an endocrine disruptor with widespread exposure and multiple effects. *J Steroid Biochem Mol Biol* 127(1–2):27–34 (2011); <http://dx.doi.org/10.1016/j.jsbmb.2011.05.002>.

^v Ruhlen RL, et al. Low phytoestrogen levels in feed increase fetal serum estradiol resulting in the “fetal estrogenization syndrome” and obesity in cd-1 mice. *Environ Health Perspect* 116(3):322–328 (2008); <http://dx.doi.org/10.1289/ehp.10448>.

^{vi} Chamorro-García R, et al. Bisphenol A diglycidyl ether induces adipogenic differentiation of multipotent stromal stem cells through a peroxisome proliferator activated receptor gamma-independent mechanism. *Environ Health Perspect*; <http://dx.doi.org/10.1289/ehp.1205063> [online 25 May 2012].

^{vii} CDC. Fourth Report on Human Exposure to Environmental Chemicals, 2009. Atlanta, GA:U.S. Department of Health and Human Services, Centers for Disease Control and Prevention. Available: <http://www.cdc.gov/exposurereport/> [accessed 25 Jun 2012].

^{viii} Shim WS, et al. The long-term effects of rosiglitazone on serum lipid concentrations and body weight. *Clin Endocrinol (Oxf)* 65(4):453–459 (2006); <http://dx.doi.org/10.1111/j.1365-2265.2006.02614>.

^{ix} Smith SR, et al. Effect of pioglitazone on body composition and energy expenditure: a randomized controlled trial. *Metabolism* 54(1):24–32 (2005); <http://dx.doi.org/10.1016/j.metabol.2004.07.008>.

^x Metabolic setpoint refers to a range of body weights that are the norm for an individual. Under the setpoint hypothesis, weight loss or gain triggers unidentified corrective mechanisms that return the body to its setpoint, similar to the way a thermostat is used to maintain a comfortable indoor temperature regardless of the weather outdoors.

^{xi} Wing RR, Hill JO. Successful weight loss maintenance. *Annu Rev Nutr* 21:323–341 (Jul 2001); <http://dx.doi.org/10.1146/annurev.nutr.21.1.323>.