Mobilization of Environmental Toxicants Following Bariatric Surgery

Robert H. Brown [ID] [1,2], *Derek K. Ng*[3], *Kimberley Steele*[4], *Michael Schweitzer*[4], *and John D. Groopman*[2]

Objective: Persistent organic pollutants (POPs) are lipophilic environmental toxicants that accumulate in adipose tissue. Weight loss leads to mobilization and increased redistribution of these toxicants. Many are obesogens and endocrine disruptors. Increased exposure could pose long-term health risks. The study objective was to measure the changes in serum concentrations of lipophilic POPs during significant weight loss.

Methods: This study enrolled 27 patients at a university hospital in a longitudinal, 6-month, observational study examining changes in POP blood levels after bariatric surgery. The primary outcome was the changes in the concentrations of 24 polychlorinated biphenyls (PCBs), 9 organochlorine pesticides (OCPs), 11 polybrominated diphenyl ethers, 2,2′,4,4′,5,5′-hexabromobiphenyl, and 4 perfluorochemicals (PFCs).

Results: Older adults (those born before 1976) had baseline levels of PCBs, OCPs, and PFCs that were two- to fivefold higher than younger adults (those born after 1976). Older adults had greater increases in PCBs, OCPs, and polybrominated diphenyl ethers associated with weight loss. Conversely, younger adults had greater increases in PFCs associated with weight loss. On average, blood POP levels increased as weight loss occurred.

Conclusions: Although weight loss is considered beneficial, the release and redistribution of POPs to other lipid-rich organs such as the brain, kidneys, and liver warrant further investigation. Interventions should be considered to limit organ exposure to POPs when weight loss interventions are planned.

Introduction

Morbid obesity is defined by the NIH as a BMI greater than 35 kg/m^2 (1,2). More than 5% of the adult US population (more than 16,000,000 people, or close to the population of the state of Florida) now has morbid obesity (3). These individuals have increased risk of multiple chronic diseases, including diabetes, hypertension, and cancers at many organ sites, leading to higher disease burden and associated medical costs (4). In response to the obesity epidemic, more than 200,000 bariatric surgical procedures are performed annually at significant health care costs. One positive consequence of bariatric surgery is the rapid weight loss that, when maintained, can lead to the reversal of chronic conditions such as type 2 diabetes (5).

An issue that has received far less epidemiological and clinical attention is the accumulation over decades of lipophilic environmental toxicants in adipose tissue. These environmental toxicants include a spectrum of persistent organic pollutants (POPs), including polychlorinated biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs), organochlorine pesticides (OCPs), and perfluorochemicals (PFCs) (6-19). Many of these compounds are known to have endocrine-disrupting effects (20,21).

Although it promotes a healthier life, rapid weight loss may also have an insidious adverse effect because of the release of stored POPs from adipose tissue into the circulation, resulting in rising plasma concentrations that can trigger deleterious signaling pathways. In this longitudinal study, we evaluated the overall burden and mobilization of these environmental toxicants that bioaccumulated in adipose tissues at the time of bariatric surgery and over the course of several months among individuals with morbid obesity. Furthermore, we evaluated the effects of birth cohorts on the overall burden and rate of change in the serum concentrations with significant weight loss.

[1] Departments of Anesthesiology, Medicine, and Radiology, Johns Hopkins Medical Institutions, Baltimore, Maryland, USA. Correspondence: Robert H. Brown (rbrown@jhsph.edu) [2] Department of Environmental Health and Engineering, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA [3] Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA [4] Department of Surgery, Johns Hopkins Medical Institutions, Baltimore, Maryland, USA.

Methods

Inclusion criteria included being a patient with morbid obesity scheduled for laparoscopic bariatric surgery at the Johns Hopkins Center for Bariatric Surgery in Baltimore, Maryland. Patients were scheduled for routine standard follow-up visits at approximately 2 weeks, 6 weeks, 3 months, and 6 months following surgery. The study was approved by the Institutional Review Board of Johns Hopkins University. All participants provided written informed consent.

Briefly, each patient underwent a thorough history and physical examination (routine standard of care for bariatric patients) to document demographics, including age, sex, height, weight, BMI, and the absence of exclusion criteria. At the time of surgery, venous blood and urine were collected shortly after the patient was anesthetized. At each follow-up clinic visit, venous blood and urine were collected. The blood samples were allowed to clot at room temperature for at least 30 minutes. The tubes were then centrifuged for 10 minutes at 1,000*g*. The serum was transferred to brown glass bottles and cryogenic vials and stored at −30°C. After completion of the study, all samples were shipped to the Centers for Disease Control and Prevention on dry ice. For PCBs, PBDEs, and persistent pesticides, the methodology used for processing the samples included automatic fortification of the samples with internal standards using a Gilson 215 liquid handler (Gilson Inc., Middleton, Wisconsin). The samples were thereafter extracted by automated liquid-liquid extraction using the liquid handler. Removal of coextracted lipids was performed on a silica:silica/sulfuric acid column using the Rapid Trace (Biotage, Uppsala, Sweden) equipment for automation. Final analytical determination of the target analytes was performed by gas chromatography isotope dilution high-resolution mass spectrometry employing a DFS (Thermo DFS, Bremen, Germany) instrument (22). For PFCs, the analyses were conducted using a modification of the method as previously reported (23). All concentration data were reported as background subtracted; the background refers to the contamination of blank samples in the same run as the unknowns. All concentration data were corrected for the average amount present in blank samples. Three blanks were included in every set of 30 samples (24,25).

The primary outcome was the baseline levels and changes for the serum biomarkers among four toxicant domains (PCB, OCP, PBDE, and PFC) by older (born before 1976) and younger (born after 1976) individuals. To describe the differences at baseline and changes per 10 kg of weight lost and how they differed by birth cohort, separate log linear mixed-effects models (with random intercepts) for each biomarker were fit. The independent variables were birth cohort, kilograms lost at the time of biomarker measurement, and the interaction between birth cohort and kilograms lost. In addition, we also performed additional analyses of the data using age as a continuous variable (online Supporting Information). The dichotomization of age may have led to some information loss. Our additional analyses treated age as a continuous variable and scaled per 5-year increase in age.

To appropriately model the biomarker data below the limit of detection, we used previously described maximum likelihood methods by PROC NLMIXED in SAS software (version 9.4; SAS Institute, Cary, North Carolina) (26). Statistical significance was assessed at the $\alpha = 0.05$ level. Graphics were created in S-Plus 8.2 (TIBCO Software, Palo Alto, California).

Results

A total of 27 individuals were enrolled; 1 individual was excluded because of a canceled surgery. Table 1 displays the characteristics of the 26 individuals at the time of bariatric surgery. Because PCBs and

TABLE 1 Demographic and clinical characteristics of study participants at the time of bariatric surgery

	Born prior to 1976, *n* = 17	Born after 1976, *n* = 9	*P* value
Demographics			
Age at surgery, y	47 (42-50)	29 (28-34)	**<0.001**
Male	18% (3)	0% (0)	0.529
Black race	35% (6)	33% (3)	1.000
Body size characteristics			
Height, m	1.68 (1.65-1.70)	1.64 (1.60-1.70)	0.202
Weight, kg	118.9 (108.4-132.5)	122.9 (114.3-140.6)	0.500
BMI, kg/m^2	40.7 (39.3-45.9)	45.7 (44.1-47.8)	0.090
Former smoker	35% (6)	33% (3)	1.000
Comorbidities			
Hypertension	76% (13)	22% (2)	**0.014**
Diabetes mellitus	29% (5)	33% (3)	1.000
Hyperlipidemia	41% (7)	11% (1)	0.190
Metabolic syndrome	18% (3)	0% (0)	0.529
Anxiety or depression	47% (8)	33% (3)	0.683
Asthma	12% (2)	22% (2)	0.591
Fatty liver disease	6% (1)	0% (0)	1.000
Hypothyroidism	6% (1)	0% (0)	1.000

Data shown as median (interquartile range) or percent (frequency). *P* for differences based on rank sum test for continuous variables and Fisher exact test for categorical variables. Bolded values denote statistical significance.

dichlorodiphenyltrichloroethane were banned by the US Environmental Protection Agency during the mid-1970s, individuals were grouped by putative higher and lower exposure according to birth before and after 1976, respectively. The median presurgical BMI was 42.9 kg/m² (median weight 122 kg; Figure 1). The cohort lost an average of 23.4%±5.7% of their total weight over the approximately 6 months of observation (to 32.6 kg/m²; Figure 1). The rates of loss were comparable among all participants.

In total, 109 blood samples (out of a possible total 130 samples, or 84%) were analyzed for 49 separate POPs over five time points: 24 PCBs, 9 OCPs, 4 PFCs, and 11 PBDEs. At baseline, 24 PCBs, 5 OCPs, 8 PBDEs, and 4 PFCs had detectable levels. Samples with undetectable POPs were considered below the level of analytical detection (i.e., POP serum levels were treated as not absent but rather treated as not detectable by the assay), thus undetectable POPs were not a reflection of no environmental exposure (27). The baseline serum concentrations for these POPs were all within or below the levels reported in the National Health and Nutrition Examination Survey (NHANES) (27). Table 2 presents the median values for each POP measured at the time of surgery (baseline) and the within-person maximum levels during the course of follow-up.

For 21 of the 24 PCBs, levels of PCBs were approximately fivehold higher in the pre-1976 compared with the post-1976 group (Figure 2A). We observed that, for all but two of the PCB congeners measured, there was a significantly higher serum level in the older group. For the two PCB congeners that did not show a difference between the age groups (PCB 28 and PCB66; Figure 2A), it was likely due to the approximately threefold-greater number of samples that were below the limit of detection in the older group compared with the younger group. There were similar age-dependent results at baseline for OCPs and PFCs, with

higher levels observed in the pre-1976 compared with the post-1976 group (Figure 2B-2D), ranging from 1.40- to 3.11-fold higher OCP levels and 1.98- to 2.44-fold higher PFC levels. In contrast, we found no difference in PBDE levels between the two groups (Figure 2C).

The magnitude of the increase in serum toxicants with weight loss varied by age group. For PCBs, there was a greater increase in serum levels per 10 kg of loss in weight for the pre-1976 group compared with the post-1976 group with the exception of PCB167 (Figure 3A). There was an overall higher rate of increase in PCB serum levels in addition to higher baseline levels, although the differences in the rates of change with weight loss did not appear to be correlated with the initial baseline levels among the various congeners (Figure 2A and Figure 3A).

Across all PCBs measured, in the older group there was a narrow range of increase in PCB concentrations of approximately 10% per 10 kg of weight lost, but all were significant. In contrast, for the younger group, across the PCB congener concentrations, the rates of increase were wider, ranging from −2% to 15% for each 10 kg of weight lost (Figure 3A). To our knowledge, the current study is the first to measure as many as 24 PCB congeners at multiple time points at the point of the greatest rate of weight loss after bariatric surgery.

For OCPs, the rates of change in serum concentrations with weight loss were also greater in the older compared with the younger age group for all OCPs (Figure 3B) despite similar baseline levels. However, the differences in the rates of change with weight loss did not appear to correlate with the initial baseline levels among the various OCPs (Figure 3B).

The rates of increase in PBDE serum concentrations were again different in the older versus the younger group (Figure 3C). For the older
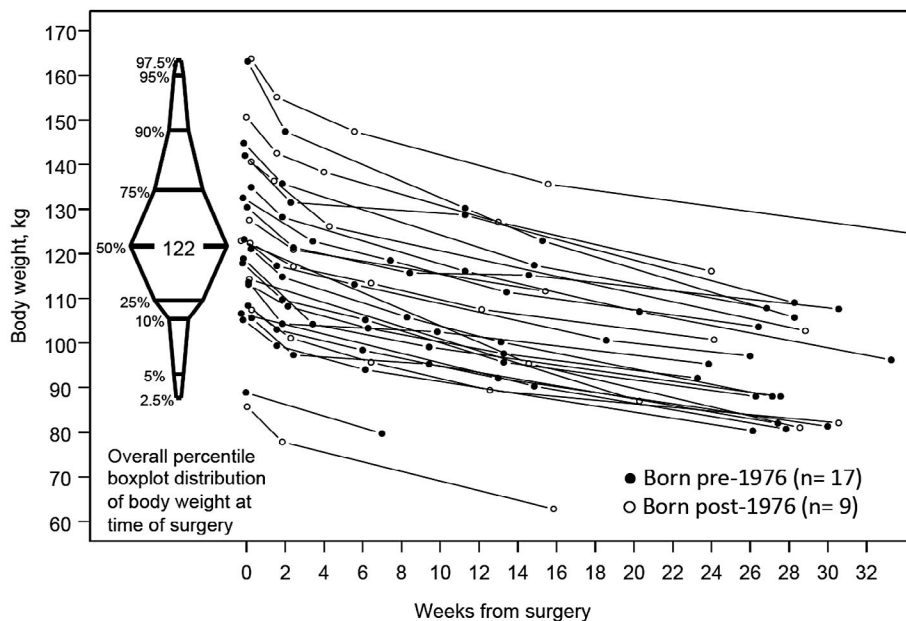
Figure 1 Box plot of the baseline body weight (kilograms) of the participants (left side) and the individual starting weight and change in weight at each clinic visit by the week post surgery (right). Open circles represent post-1976 ("younger") group, and closed circles represent pre-1976 ("older") group. For one participant, the last measurement was 42 weeks post surgery.

TABLE 2 Descriptive statistics of all samples in which POPs were measured in this study of 26 participants who underwent bariatric surgery

Variable	Number of samples	Percent detectable	Minimum	25th percentile	Median	75th percentile	Maximum
PCB (ng/g lipid)							
PCB28	104	74.0%	0.340	0.477	0.702	1.463	7.439
PCB66	105	84.8%	0.200	0.356	0.514	0.765	5.605
PCB74	105	100.0%	0.720	1.458	2.522	4.882	22.600
PCB99	104	100.0%	0.640	1.365	2.685	5.811	33.520
PCB105	102	98.0%	0.220	0.678	1.080	1.616	15.530
PCB114	104	64.4%	0.120	0.204	0.348	0.728	2.259
PCB118	99	100.0%	1.306	3.216	5.391	9.279	61.130
PCB146	103	97.1%	0.120	0.750	1.582	4.008	12.760
PCB153	105	100.0%	1.294	6.131	13.050	33.950	108.300
PCB156	105	95.2%	0.157	0.796	1.750	3.649	12.070
PCB157	105	74.3%	0.120	0.240	0.423	0.896	3.247
PCB167	93	82.8%	0.120	0.265	0.619	1.344	5.495
PCB170	81	98.8%	0.190	1.459	2.946	7.241	19.170
PCB178	100	79.0%	0.120	0.262	0.541	1.337	3.880
PCB180	105	100.0%	0.475	3.288	6.987	15.050	51.120
PCB183	96	92.7%	0.120	0.454	0.882	2.563	9.184
PCB187	98	95.9%	0.149	1.405	2.844	6.894	21.090
PCB189	104	36.5%	0.120	0.180	0.210	0.318	1.064
PCB194	101	93.1%	0.120	0.500	1.382	3.140	9.064
PCB199	103	93.2%	0.120	0.693	1.558	4.382	10.640
PCB206	104	93.3%	0.120	0.593	1.165	3.113	6.913
PCB209	105	77.1%	0.120	0.250	0.583	1.676	5.619
PCB138_158	103	100.0%	1.161	4.609	9.141	19.510	97.270
PCB196_203	104	94.2%	0.161	0.710	1.583	4.320	11.480
OCP (ng/g lipid)							
p,p'-DDT	105	86.7%	0.810	1.230	1.666	2.230	7.457
p,p'-DDE	106	100.0%	18.600	44.470	68.405	210.300	660.300
Oxychlordane	105	99.0%	0.919	2.766	4.841	13.810	68.380
HCB	105	100.0%	3.462	5.823	8.268	11.510	24.100
Trans-nonochlor	81	100.0%	1.154	4.438	7.311	18.970	129.000
PBDE (ng/g lipid)							
PBDE28	105	94.3%	0.164	0.447	0.884	1.339	4.919
PBDE47	105	100.0%	1.595	5.849	12.740	21.200	81.130
PBDE85	105	66.7%	0.150	0.200	0.270	0.419	1.872
PBDE99	105	93.3%	0.250	0.759	1.846	4.392	14.740
PBDE100	105	100.0%	0.298	1.495	2.675	5.953	42.240
PBDE153	105	100.0%	0.923	2.444	4.117	7.986	160.100
PBDE154	105	59.0%	0.150	0.200	0.242	0.488	2.373

TABLE 2 (continued).

Variable	Number of samples	Percent detectable	Minimum	25th percentile	Median	75th percentile	Maximum
PBDE209	105	61.0%	0.750	1.000	1.204	1.668	22.820
PFC (ng/mL)							
PFOS	104	100.0%	1.600	2.450	3.950	8.100	33.500
PFOA	104	100.0%	0.500	1.100	1.650	2.750	16.300
PFDEA	104	92.3%	0.100	0.200	0.300	0.500	2.500
PFNA	104	100.0%	0.300	0.600	0.950	1.550	6.200

Samples were not independent such that these numbers represent repeated samples within individuals over the course of follow-up. DDT, dichlorodiphenyltrichloroethane; DDE, dichlorodiphenyldichloroethylene; HCB, hexachlorobenzene; OCP, organochlorine pesticide; PBDE, polybrominated diphenyl ether; PCB, polychlorinated biphenyl; PFC, perfluorochemical; PFDEA, perfluorodecanoic acid; PFNA, perfluorononanoic acid; PFOA, perfluorooctanoic acid; PFOS, perfluorooctanesulfonic acid.

group, the increase in PBDE concentrations for each 10 kg of weight lost ranged from approximately 13% to 23%. For the younger group, the rates of increase in PBDE concentrations ranged from 0% to 14% for each 10 kg of weight lost. At present, it is unclear what would cause this greater increase in the serum concentrations with similar baseline PBDE levels for the older versus the younger individuals.

In contrast, for PFCs, we saw a very different response to weight loss. For these toxicants, we found minimal changes in serum levels per 10 kg of weight lost for the pre-1976 group and the post-1976 group (Figure 3D). Furthermore, in complete distinction from the other POPs that we measured, we found higher rates of increase in serum levels with weight loss for the younger compared with the older group (Figure 3D).

Discussion

We found that older compared with younger adults with morbid obesity had levels of PCBs, OCPs, and PFCs approximately two- to fivefold higher at the time of bariatric surgery. More importantly, with rapid weight loss, older adults had greater increases in serum levels of the lipid-accumulating environmental toxicants PCBs, OCPs, and PBDEs. In contrast, PFCs, which bioconcentrate in the serum, kidneys, and liver (28,29), showed a completely different response to weight loss. While the older group had higher baseline concentrations, the younger group had a greater increase in the PFC serum levels associated with weight loss. It is important to note that our "older" group was still relatively young, with a mean age of only 47 years. Therefore, they have the prospect, especially after weight loss, of living several more decades with increased exposure to these toxicants.

With weight gain, exposure to lipophilic POPs results in the bioaccumulation and dilution of these toxicants in adipose tissue that are not readily bioavailable. However, weight loss can lead to remobilization and increased levels of these compounds in the blood, resulting in increased bioactivity at sensitive organs. The toxicology of these agents might have deleterious consequences through several signaling pathways and resultant feedback loops. The goal of the work described here was to provide insights into the rapid mobilization of these toxicants from fat storage and provide baseline data for clinical and epidemiological follow-up investigations.

PCBs are very resistant to degradation, oxidation, acids, bases, and other chemical agents and are thermally stable. In the late 1970s, the Environmental Protection Agency limited the production and disposal of PCBs and eventually banned their manufacture in 1979. Food is the main nonoccupational source of exposure for the general population (30), through the ingestion of fatty foods such as dairy products and fish. Breastfeeding is another major source of exposure for infants (31-33). Most OCPs were banned for use in the US in the 1970s and 1980s, yet some are still used in other parts of the world (34). Industrial production of PFCs was discontinued in 2002, but they are still produced in China (35). Human exposure routes include air, indoor dust, water, food, and numerous consumer products. Unlike other persistent chemicals, PFCs do not tend to accumulate in fat tissue but still can have long residence times in the body (36). PBDEs were voluntarily phased out of production in the US between 2004 and 2013 (37). Human exposure to PBDEs is thought to result from dietary sources, including fish, fatty foods, mother's milk, and dust (38,39).
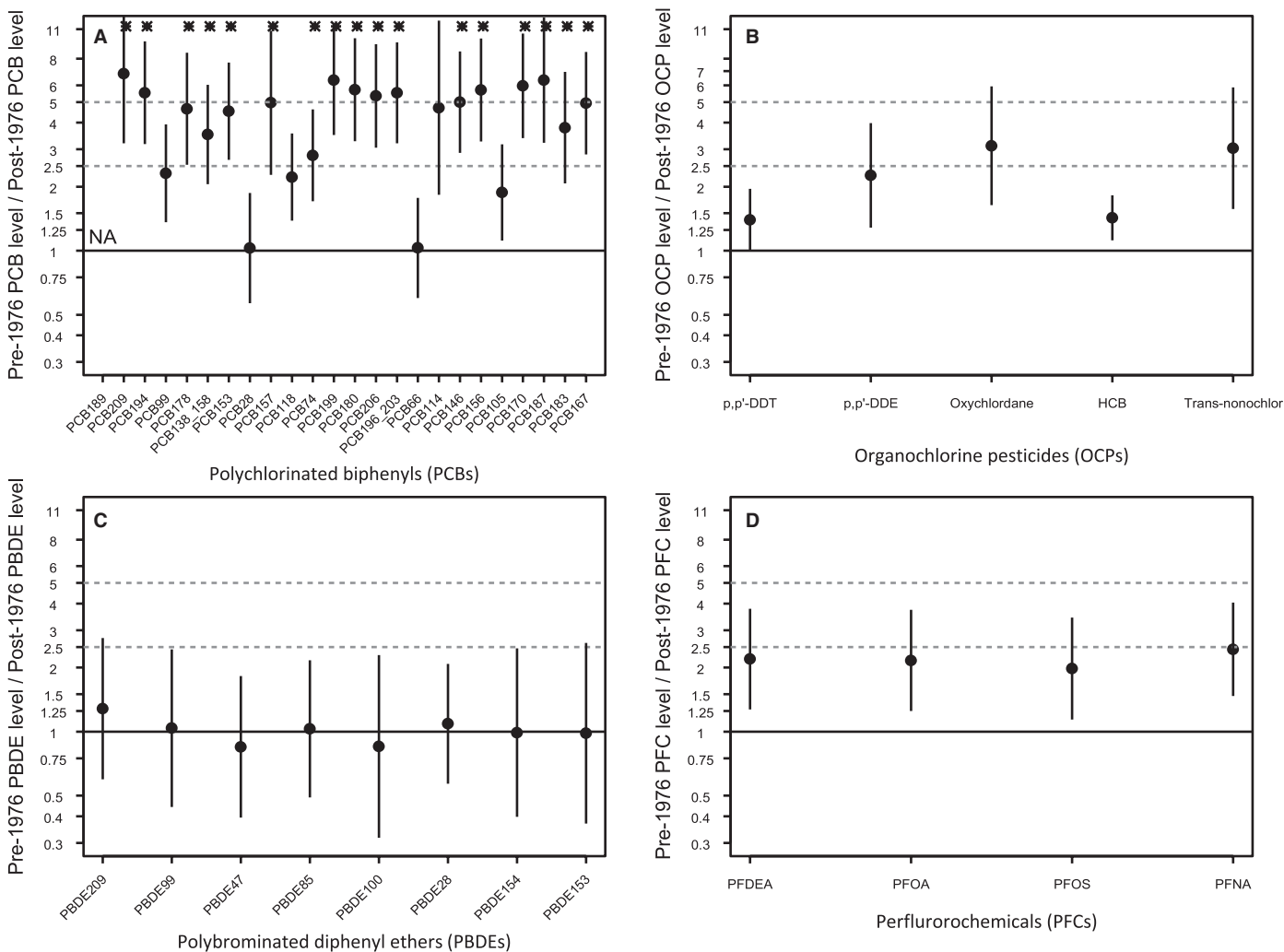
Figure 2 Ratio of geometric mean POP levels at baseline for the pre-1976 group relative to the post-1976 group arranged in order of lowest to highest POP change in serum level with weight loss in the post-1976 group. Pre-1976 compound levels refer to the average levels among participants born prior to 1976, and post-1976 compound levels refer to the average levels among participants after 1976. (**A**) PCB levels, (**B**) OCP levels, (**C**) PBDE levels, and (**D**) PFC levels. Asterisks represents *P* for difference comparing pre-1976 versus post-1976: ✱*P* < 0.001.

The major concern for all POPs is their effect on hormone action. They are collectively known as endocrine disruptors. Like hormones, endocrine disruptors exhibit complex dose-response curves and can act at extremely low concentrations. Because of the changing levels of hormones throughout the life cycle, endocrine disruptors can have profound immediate and latent effects. The mechanisms of action of endocrine disruptors are multiple and complex (20,21). Endocrine disruptors negatively affect obesity, diabetes mellitus, cardiovascular diseases, female reproduction, male reproduction, hormone-sensitive cancers in females, the prostate gland, the thyroid gland, and neurodevelopment (20,21). With the rapid increased POP serum levels with weight loss, this may lead to an increased redistribution of these POPs to other lipid-rich tissues such as the brain, heart, kidneys, and liver, with potential toxic effects (40,41). Whether the increased concentrations of certain POPs compared with others carry increased health risks remains to be determined.

Recently, POPs have been reported to be obesogens. Obesogens can be functionally defined as chemicals that alter homeostatic metabolic set

points, disrupt appetite controls, perturb lipid homeostasis to promote adipocyte hypertrophy, stimulate adipogenic pathways that enhance adipocyte hyperplasia, or otherwise alter adipocyte differentiation during development (42,43). Data in adult rodent models using chronic exposures to mixtures of POPs led to increased visceral fat (44,45). Malarvannan et al. measured multiple POPs in the visceral and subcutaneous fat compartments. They showed that, in patients who had morbid obesity, the percentage of subcutaneous fat was significantly greater than visceral fat (46). Because they found that the absolute POP levels were not different between the two fat compartments, they inferred that a higher level of selected POPs in adipose tissue seems to predispose one to the accumulation of visceral adiposity (46).

If people who are lean and who have obesity have equal total body burden of POPs, POP serum concentrations in persons with obesity are expected to be lower than in persons who are lean because of the dilution effects of adipose tissue mass (43,47). Assuming a greater POP intake for individuals with obesity through diet, the lower POP serum
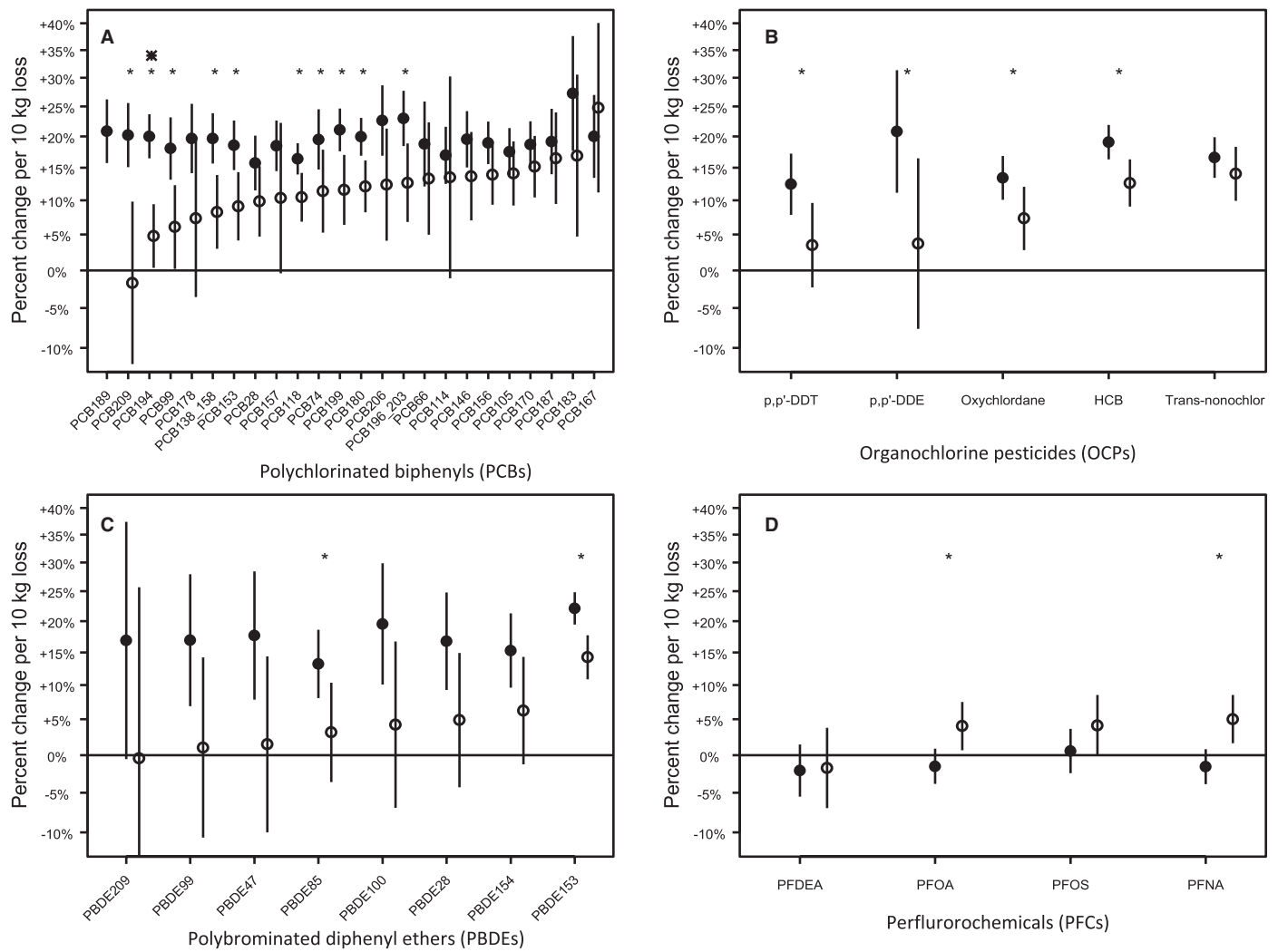
Figure 3 Percent change in POPs per 10 kg of weight lost for the pre-1976 (closed circles) and post-1976 (open circles) groups. POPs are arranged in order of lowest to highest POP change in serum level with weight loss in the post-1976 group. (A) The percent change in PCB, (B) percent change in OCP, (C) percent change in PBDE, and (D) percent change in PFC. Asterisks represents *P* for difference comparing pre-1976 versus post-1976: *$P < 0.05$, ✳*$P < 0.001$*.

levels at baseline in individuals with obesity compared with individuals who are lean may be explained by body dilution because of a higher fat content (47). Changes in POPs were shown to be inversely associated with changes in weight (48). Weight loss is responsible for increasing POP serum concentrations because of the reduction in storage capacity in the adipose tissue compartment and the release of POPs into blood. After significant weight loss, when going from having morbid obesity (Class 3 obesity) to simple obesity (Class 1 obesity), serum levels of individuals with obesity were shown to increase to levels greater than those of lean individuals (47). In our participants, even after a significant amount of weight loss, the majority of the POP concentrations remained within the range of the most recently released NHANES values (2003-2004). However, several issues remain. First, while there was a ~25% weight loss, the individuals continued, on average, to have morbid obesity. If these people continued to lose weight and reached a normal body habitus of BMI 25, we calculated that their mean group values for the vast majority of their PCB and PFC levels would be

substantially higher than the mean NHANES levels (data not shown), while the calculated OCP and PBDE levels would be similar to those of NHANES (data not shown). Also, the pathophysiological effects of a rapid increase in POP levels in the serum may not have the same effects on end organs as a slow rise. In addition, no "safe" levels for these POPs have been determined; the risk of increasing serum levels and organ exposure remains to be determined.

There are several unique strengths of this current work. One is that longitudinal measurements of POP concentrations were obtained, both prior to surgery and for a substantial period of time after surgery (6 months), when most of the weight loss occurs. Furthermore, multiple POPs were measured. Because exposure to POPs is never from a single agent, focusing on an individual POP may be misleading. Health outcomes likely reflect the mixture of multiple POPs. Thus, a more robust analysis examining multiple POPs at the same time as we did may become necessary to ascribe causality. Another strength of our study was the use of the

Centers for Disease Control and Prevention analytical laboratories to perform all the blood serum measurements. These are Clinical Laboratory Improvement Amendments-certified laboratories that ensured the quality of the laboratory testing. In addition, these are the same laboratories that perform the NHANES measurements of the same environmental toxicants. This assures comparability with the levels of toxicants in the general population. Another strength of this study was the collection at multiple time points. This allowed us to compare the changes in weight with the changes in POP concentrations. The outcomes were analyzed independently, which allowed for the most flexible approach to identify POP congeners that were different. We used appropriate analysis of limit-of-detection issues that allowed for left-censored data. Lastly, weight loss, rather than time from surgery, was the primary independent variable and provided a standardized approach that reflected the biological action of interest (i.e., changes in serum concentrations of lipophilic chemicals that were modified by rapid fat loss) and allowed for heterogeneity of individual weight loss.

There were several limitations to the study. The sample size was relatively small, with only 26 participants in total. Even when we divided the participants into those born before and after 1976, and with only nine individuals in one group, we still observed relatively large effect sizes. In addition, we performed multiple comparisons. Although this study involved several different biomarkers, we did not include formal adjustments for multiple comparisons because we hypothesized that weight-associated biomarker changes would show a biologically coherent pattern. In particular, we hypothesized that weight would be reflected by increases in all lipid-stored biomarkers. This biologically coherent pattern dictates that results should be mutually reinforcing, rather than a series of independent tests. Therefore, formal multiple-comparisons adjustments such as the Bonferroni method would not be appropriate (49). In addition, we assumed that linear changes were related to outcomes. Also, the duration of the follow-up was only 6 months post bariatric surgery. While the majority of the weight loss generally occurs in the first 6 months after surgery, further investigation is needed to describe these dynamics after the body mass has stabilized. We studied only individuals who lost weight through bariatric surgery. While other methods of weight loss such as restricted diets are not as effective, whether the changes we saw in the POP serum concentrations would increase as much with a slower loss in weight remains to be determined.

Obesity is associated with increased morbidity and mortality, and losing weight has clear positive healthy consequences. With a large and rapid loss in weight after bariatric surgery, we observed a concomitant large increase in the POP serum concentrations that are stored in adipose tissue. POPs are ubiquitous in our environment and in our bodies. Although the benefits of weight loss are well documented, there is a potential negative aspect to losing weight in terms of potential release and redistribution of POPs to other lipid-rich organs such as the brain, kidneys, and liver. Further research is needed to investigate whether there are potential short- or long-term risks and consequences because of these increased exposures. If significant potential risk is identified, leading to long-term consequences, possible interventions should be considered to increase excretion of and limit increased exposure to POPs when weight loss interventions are planned.**O**

Acknowledgments

References

1. Berrington de Gonzalez A, Hartge P, Cerhan JR, et al. Body-mass index and mortality among 1.46 million white adults. *N Engl J Med* 2010;363:2211-2219.
2. US Department of Health and Human Services. NIH study identifies ideal body mass index. National Institutes of Health website. https://www.nih.gov/news-events/news-releases/nih-study-identifies-ideal-body-mass-index. Published December 1, 2010. Accessed August 1, 2018.
3. Sturm R, Hattori A. Morbid obesity rates continue to rise rapidly in the United States. *Int J Obes (Lond)* 2013;37:889-891.
4. Centers for Disease Control and Prevention. Adult obesity causes & consequences. https://www.cdc.gov/obesity/adult/causes.html. Updated August 29, 2017. Accessed August 12, 2019.
5. Lewis KH, Arterburn DE, Zhang F, et al. Comparative effectiveness of vertical sleeve gastrectomy versus Roux en Y gastric bypass for diabetes treatment: a claims-based cohort study [published online June 12, 2019]. *Ann Surg.* doi:10.1097/SLA.0000000000003391
6. Antignac JP, Cariou R, Zalko D, et al. Exposure assessment of French women and their newborn to brominated flame retardants: determination of tri- to deca- polybromodiphenylethers (PBDE) in maternal adipose tissue, serum, breast milk and cord serum. *Environ Pollut* 2009;157:164-173.
7. Covaci A, Voorspoels S, Roosens L, Jacobs W, Blust R, Neels H. Polybrominated diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs) in human liver and adipose tissue samples from Belgium. *Chemosphere* 2008;73:170-175.
8. Kalantzi OI, Brown FR, Caleffi M, Goth-Goldstein R, Petreas M. Polybrominated diphenyl ethers and polychlorinated biphenyls in human breast adipose samples from Brazil. *Environ Int* 2009;35:113-117.
9. Kannan K, Reiner JL, Yun SH, et al. Polycyclic musk compounds in higher trophic level aquatic organisms and humans from the United States. *Chemosphere* 2005;61:693-700.
10. Kunisue T, Takayanagi N, Isobe T, et al. Polybrominated diphenyl ethers and persistent organochlorines in Japanese human adipose tissues. *Environ Int* 2007;33:1048-1056.
11. Moon HB, Lee DH, Lee YS, Kannan K. Occurrence and accumulation patterns of polycyclic aromatic hydrocarbons and synthetic musk compounds in adipose tissues of Korean females. *Chemosphere* 2012;86:485-490.
12. Petreas M, Nelson D, Brown FR, Goldberg D, Hurley S, Reynolds P. High concentrations of polybrominated diphenylethers (PBDEs) in breast adipose tissue of California women. *Environ Int* 2011;37:190-197.
13. Schiavone A, Kannan K, Horii Y, Focardi S, Corsolini S. Polybrominated diphenyl ethers, polychlorinated naphthalenes and polycyclic musks in human fat from Italy: comparison to polychlorinated biphenyls and organochlorine pesticides. *Environ Pollut* 2010;158:599-606.
14. Wang N, Kong D, Shan Z, et al. Simultaneous determination of pesticides, polycyclic aromatic hydrocarbons, polychlorinated biphenyls and phthalate esters in human adipose tissue by gas chromatography-tandem mass spectrometry. *J Chromatogr B Analyt Technol Biomed Life Sci* 2012;898:38-52.
15. Hirai T, Fujimine Y, Watanabe S, Nakano T. Distribution of polybrominated diphenyl ethers in Japanese autopsy tissue and body fluid samples. *Environ Sci Pollut Res Int* 2012;19:3538-3546.
16. Kunisue T, Johnson-Restrepo B, Hilker DR, Aldous KM, Kannan K. Polychlorinated naphthalenes in human adipose tissue from New York, USA. *Environ Pollut* 2009;157:910-915.
17. Moon HB, Lee DH, Lee YS, Choi M, Choi HG, Kannan K. Polybrominated diphenyl ethers, polychlorinated biphenyls, and organochlorine pesticides in adipose tissues of Korean women. *Arch Environ Contam Toxicol* 2012;62:176-184.
18. Pulkrabova J, Hradkova P, Hajslova J, Poustka J, Napravnikova M, Polacek V. Brominated flame retardants and other organochlorine pollutants in human adipose tissue samples from the Czech Republic. *Environ Int* 2009;35:63-68.
19. Crinnion WJ. The CDC Fourth National Report on Human Exposure to Environmental Chemicals: what it tells us about our toxic burden and how it assist environmental medicine physicians. *Altern Med Rev* 2010;15:101-109.
20. Gore AC, Chappell VA, Fenton SE, et al. EDC-2: The Endocrine Society's second scientific statement on endocrine-disrupting chemicals. *Endocr Rev* 2015;36:E1-E150.
21. Gore AC, Chappell VA, Fenton SE, et al. Executive summary to EDC-2: The Endocrine Society's second scientific statement on endocrine-disrupting chemicals. *Endocr Rev* 2015;36:593-602.
22. Jones R, Edenfield E, Anderson S, Zhang Y, Sjokin A. Semi-automated extraction and cleanup method for measuring persistent organic pollutants in human serum. *Organohalogen Compounds* 2012;74:97-98.
23. Kato K, Basden BJ, Needham LL, Calafat AM. Improved selectivity for the analysis of maternal serum and cord serum for polyfluoroalkyl chemicals. *J Chromatogr A* 2011;1218:2133-2137.
24. Sjodin A, McGahee EE 3rd, Focant JF, et al. Semiautomated high-throughput extraction and cleanup method for the measurement of polybrominated diphenyl ethers and polybrominated and polychlorinated biphenyls in breast milk. *Anal Chem* 2004;76:4508-4514.
25. Sjodin A, Schecter A, Jones R, et al. Polybrominated diphenyl ethers, 2,2′,4,4′,5,5′-hexachlorobiphenyl (PCB-153), and p, p'-dichlorodiphenyldichloroethylene (p, p'-DDE)

concentrations in sera collected in 2009 from Texas children. *Environ Sci Technol* 2014;48:8196-8202.

26. Egner PA, Chen JG, Zarth AT, et al. Rapid and sustainable detoxication of airborne pollutants by broccoli sprout beverage: results of a randomized clinical trial in China. *Cancer Prev Res (Phila)* 2014;7:813-823.

27. Centers for Disease Control and Prevention. National Report on Human Exposure to Environmental Chemicals, Updated Tables. https://www.cdc.gov/exposurereport/. Accessed October 1, 2018.

28. US Environmental Protection Agency. Long-chain perfluorinated chemicals (PFCs): action plan. https://www.epa.gov/sites/production/files/2016-01/documents/pfcs_action_plan1230_09.pdf. Published December 30, 2009. Accessed October 1, 2018.

29. US Environmental Protection Agency. Drinking water health advisory for perfluorooctane sulfonate (PFOS). https://www.epa.gov/sites/production/files/2016-05/documents/pfos_health_advisory_final_508.pdf. Published May 2016. Accessed October 1, 2018.

30. Centers for Disease Control and Prevention. Biomonitoring summary: non-dioxin-like polychlorinated biphenyls. https://www.cdc.gov/biomonitoring/NDL-PCBs_BiomonitoringSummary.html. Updated April 7, 2017. Accessed August 1, 2018.

31. Fang J, Nyberg E, Bignert A, Bergman A. Temporal trends of polychlorinated dibenzo-p-dioxins and dibenzofurans and dioxin-like polychlorinated biphenyls in mothers' milk from Sweden, 1972-2011. *Environ Int* 2013;60:224-231.

32. Lignell S, Winkvist A, Bertz F, et al. Environmental organic pollutants in human milk before and after weight loss. *Chemosphere* 2016;159:96-102.

33. van den Berg M, Kypke K, Kotz A, et al. WHO/UNEP global surveys of PCDDs, PCDFs, PCBs and DDTs in human milk and benefit-risk evaluation of breastfeeding. *Arch Toxicol* 2017;91:83-96.

34. Yadav IC, Devi NL, Syed JH, et al. Current status of persistent organic pesticides residues in air, water, and soil, and their possible effect on neighboring countries: a comprehensive review of India. *Sci Total Environ* 2015;511:123-137.

35. World Aluminium. Life Cycle Inventory Data And Environmental Metrics For The Primary Aluminium Industry: 2015 Data. http://www.world-aluminium.org/media/filer_public/2018/02/19/lca_report_2015_final_26_june_2017.pdf. Published June 2017. Accessed January 1, 2019.

36. Centers for Disease Control and Prevention. Biomonitoring summary: perfluorochemicals. https://www.cdc.gov/biomonitoring/PFAS_BiomonitoringSummary.html. Updated April 7, 2017. Accessed August 1, 2018.

37. US Environmental Protection Agency. Technical fact sheet: polybrominated diphenyl ethers (PBDEs). https://www.epa.gov/sites/production/files/2014-03/documents/ffrrofactsheet_contaminant_perchlorate_january2014_final_0.pdf. Published November 2017. Accessed August 1, 2018.

38. Centers for Disease Control and Prevention Biomonitoring summary: polybrominated diphenyl ethers and 2,2′,4,4′,5,5′-hexabromobiphenyl (BB-153). https://www.cdc.gov/biomonitoring/PBDEs_BiomonitoringSummary.html. Updated April 7, 2017. Accessed August 1, 2018.

39. Sjodin A, Papke O, McGahee E, et al. Concentration of polybrominated diphenyl ethers (PBDEs) in household dust from various countries. *Chemosphere* 2008;73(1 Suppl):S131-S136.

40. Jandacek RJ, Anderson N, Liu M, Zheng S, Yang Q, Tso P. Effects of yo-yo diet, caloric restriction, and olestra on tissue distribution of hexachlorobenzene. *Am J Physiol Gastrointest Liver Physiol* 2005;288:G292-G299.

41. Ohmiya Y, Nakai K. Effect of starvation on excretion, distribution and metabolism of DDT in mice. *Tohoku J Exp Med* 1977;122:143-153.

42. Janesick AS, Blumberg B. Obesogens: an emerging threat to public health. *Am J Obstet Gynecol* 2016;214:559-565.

43. Lee DH, Porta M, Jacobs DR Jr, Vandenberg LN. Chlorinated persistent organic pollutants, obesity, and type 2 diabetes. *Endocr Rev* 2014;35:557-601.

44. Ibrahim MM, Fjaere E, Lock EJ, et al. Chronic consumption of farmed salmon containing persistent organic pollutants causes insulin resistance and obesity in mice. *PLoS One* 2011;6:e25170. doi:10.1371/journal.pone.0025170

45. Ruzzin J, Petersen R, Meugnier E, et al. Persistent organic pollutant exposure leads to insulin resistance syndrome. *Environ Health Perspect* 2010;118:465-471.

46. Malarvannan G, Dirinck E, Dirtu AC, et al. Distribution of persistent organic pollutants in two different fat compartments from obese individuals. *Environ Int* 2013;55:33-42.

47. Dirtu AC, Dirinck E, Malarvannan G, et al. Dynamics of organohalogenated contaminants in human serum from obese individuals during one year of weight loss treatment. *Environ Sci Technol* 2013;47:12441-12449.

48. Lim JS, Son HK, Park SK, Jacobs DR Jr, Lee DH. Inverse associations between long-term weight change and serum concentrations of persistent organic pollutants. *Int J Obes (Lond)* 2011;35:744-747.

49. Bacchetti P. Peer review of statistics in medical research: the other problem. *BMJ* 2002;324:1271-1273.