Perspectives Correspondence

Bisphenol A and Risk Assessment

In a recent article, vom Saal and Hughes (2005) proposed that a new risk assessment on bisphenol A (BPA) is needed because of the availability of extensive new literature, including "recent epidemiologic evidence that BPA is related to disease in women." Specifically, the only research that vom Saal and Hughes cited as evidence relating BPA to disease is a study by Takeuchi et al. (2004), which they describe as a case–control study that reports that ovarian disease in women is related to blood levels of BPA.

Vom Saal and Hughes (2005) have misrepresented the Takeuchi study (Takeuchi et al. 2004): It is not a case–control study, and it does not demonstrate that BPA is specifically associated with ovarian disease.

Takeuchi et al. (2004) conducted a small cross-sectional descriptive study that assessed 73 women with respect to serum BPA, hormone concentrations, and their clinical condition at a single point in time. Women were categorized clinically as normal (either obese or nonobese), or as having hyperprolactinemia, hypothalamic amenorrhea, or polycystic ovary syndrome (PCOS) (again, either obese or nonobese). The six groups in the study each contained as many as 19 subjects (nonobese normal group) and as few as 6 subjects (PCOS obese group). The authors reported that serum BPA was higher in women with PCOS (both obese and not obese) and obese normal women than normal women who were not obese. There were also significant positive correlations between serum BPA and various androgens. Takeuchi et al. (2004) concluded that there is a strong relationship between serum BPA and androgen, and they noted that there are a number of possible explanations for this relationship.

Takeuchi et al. (2004) appropriately acknowledged that their study was a hypothesis-generating study and they did not attempt to draw conclusions about causal relationships.

Vom Saal and Hughes (2005) overstated the importance of this low-level epidemiologic evidence by referring to it as a case–control study. A case–control study is a more rigorous epidemiologic study in which a group of cases (i.e., with the disease of interest) is compared to a group of controls (i.e., without the disease of interest) with respect to exposures that occurred before the development of disease. Rather, Takeuchi et al. (2004) conducted a cross-sectional study in which both exposure and disease were assessed at a single point in time. When both exposure and outcome are assessed at a single point in time, it is not possible to determine whether the exposure preceded the clinical condition or whether the clinical condition affected the individual's level of exposure. A cross-sectional study cannot test hypotheses; at most, it can merely examine correlations. Furthermore, cross-sectional studies cannot control for confounding factors that may obscure the true relationship between exposure and disease (Hennekens and Buring 1987).

Vom Saal and Hughes (2005) overlooked the intended primary focus of the paper by Takeuchi et al. (2004), which is that there is a relationship between serum BPA and androgen levels. The exact nature of this relationship is not known at this time and Takeuchi et al. (2004) speculate that BPA may stimulate androgen production, or, more likely, androgen may suppress the metabolism of BPA. Consequently, women who have clinical conditions that are associated with elevated androgen (e.g., PCOS or obesity) may have elevated levels of BPA as a result of their elevated androgen. The cross-sectional study by Takeuchi et al. cannot shed light on the time course of events and, therefore, cannot address causal relationships among any of the variables studied in these women.

In addition, a number of recent studies have reported that several of the ELISA kits available for measurement of serum BPA [the analytic method used by Takeuchi et al. (2004)] overestimate BPA concentrations and exhibit considerable cross-reactivity, calling into question the validity of results generated by such methods (Fukata and Mori 2004; Fukata et al. 2003; Kawaguchi et al. 2003). Furthermore, it is well known that BPA is metabolized and eliminated rapidly (Volkel et al. 2002), so serum levels provide only a snapshot of BPA exposure within the last day. It is not meaningful to correlate an acute exposure (serum BPA at one time-point) with a chronic disease that took years to develop. Chronic exposure to BPA would have to be demonstrated and not assumed.

The Takeuchi et al. (2004) study suggests a hypothesis that could be further examined in an appropriately controlled analytic study. It should not be portrayed as recent epidemiologic evidence that demonstrates an association between blood levels of BPA and clinical disease in women.

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Bisphenol A: vom Saal and Hughes Respond

Our commentary describing the extensive new literature reporting low-dose effects of bisphenol A (BPA) in experimental animals (vom Saal and Hughes 2005) was written in response to a report from the Harvard Center for Risk Analysis (HCRA) by Gray et al. (2004), who concluded that "the weight of the evidence for low-dose effects [of BPA] is very weak." The HCRA report was funded by the American Plastics Council and involved a selective review of only 19 of a much larger number of studies that could have been reviewed. In our commentary we showed that a comprehensive review of the now extensive literature concerning studies in experimental animals that used doses of BPA within the range of human exposure led to exactly the opposite conclusion from that reached in the HCRA report (Gray et al. 2004), which was released 2.5 years after it was written.

At this time there are only two published epidemiologic studies showing a relationship between blood levels of BPA and diseases in humans. In his letter, Politch focuses his attention on a single study by Takeuchi et al. (2004) that describes a relationship between

BPA in blood and polycystic ovary disease (PCOS) in Japanese women. In a second recently published article, Sugiura-Ogasawara et al. (2005) reported a relationship between blood levels of BPA and recurrent miscarriage in Japanese women. Politch seeks to deflect attention from the central issue of our review by focusing only on the study by Takeuchi et al. (2004) and stating that such studies "cannot address causal relationships" and suggesting that "appropriately controlled" human studies are required. We are certain that readers of *Environmental Health Perspectives* (*EHP*) realize that these are criticisms that can be directed at all epidemiologic studies, which can never achieve the control required in laboratory experiments. Additionally, there is always some risk in arguing the methodologic details of a peer-reviewed publication in one field of scientific research (epidemiology) when the commentator's core expertise (biopsychology) lies elsewhere. Most importantly, based on his criticism of the levels of BPA reported in the blood of women by Takeuchi et al. (2004), Politch appears to be unaware of the large literature concerning the levels of BPA in human blood, urine, and tissues from studies conducted in different regions of the world reporting virtually identical mean and/or median values. For example, in a recent study at the Centers for Disease Control and Prevention, Calafat et al. (2005) found BPA in 95% of the human urine samples they assayed—in the same range reported in human blood in other studies (e.g., Schonfelder et al. 2002; Tan and Mohd 2003). All of this published literature is listed in a document available on the University of Missouri Endocrine Disruptor web site (Endocrine Disruptors Group 2005).

One point-of-view expressed by Politch that we strongly support is the proposition that human studies linking developmental exposure with adult disease are also required, based on the extensive evidence that the developing fetus and neonate are the most vulnerable to endocrine disruption. We hope that the planned National Children's Study will address this issue and begin to characterize which exposures are and are not consequential for human health. In the absence of such a study, which will take decades to complete, we rely on experimental studies in animals to make decisions regarding the potential hazards posed by chemicals.

Our comment that the epidemiologic evidence "adds to our concern" about the potential hazards posed to humans by BPA hardly qualifies as justification for the criticism that we "overstated the importance" of this or any other single study. Our concern about the potential hazards of BPA to humans is justified by the fact that the limited epidemiologic studies do follow and generally support

findings from over 125 experiments with laboratory animals showing that low doses of BPA cause adverse effects on a wide range of outcomes. We also pointed out in our article (vom Saal and Hughes 2005) that 100% of the studies showing significant effects of BPA in laboratory animals were funded by government agencies, and 100% of the studies funded by chemical corporations conclude that the same low doses of BPA do not cause significant effects. What is crucial in relation to the critique by Politch is that the two epidemiologic studies relating BPA in blood to diseases in women are consistent with the findings from studies of the hazards of BPA in animals at doses that lead to blood levels in animals within and below those detected in human blood.

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The Human Population: Accepting Species Limits

In "The Population Equation: Balancing What We Need with What We Have," Dahl (2005) presented generally accepted thought

and consensually validated data regarding the human population, even though he did not include an adequate scientific theory of absolute human population numbers. Dahl also appeared to confirm the wide agreement among scientists that it is difficult to make theoretical advances or conduct human population research because humankind is seen as essentially different from other species and the human world is viewed as being composed of many intricately connected things that interact in extremely complex ways. Therefore, the population dynamics of *Homo sapiens* are effectively relegated to the preternatural realm and are believed to include a number of factors that are so complicated and enormous as to be unsuitable for empirical research or else unknowable.

A theory of human population numbers that could objectively explain the increase and decrease of the human population would be useful. Perhaps correlation data from Hopfenberg and Pimentel (2001) and the recent mathematical formulation of this biologic phenomenon by Hopfenberg (2003) provide a basis for an apparently unexpected theoretical perspective. According to the empirical research (Hopfenberg 2003), human population growth is a rapidly cycling positive feedback loop in which food availability drives population growth and this growth in human numbers gives rise to the mistaken impression that food production needs to be increased even more.

The data of Hopfenberg (2003) and Hopfenberg and Pimentel (2001) indicate that the world's human population—all segments of it—grows by approximately 2% per year, including more people with brown eyes and more with blue eyes; more tall people and more short people; and more people who grow up well fed and more who grow up hungry. We may or may not be reducing hunger by increasing food production; however, we are most certainly producing more and more hungry people. The evidence suggests that the remarkably successful efforts of humankind to increase food production to feed a growing population results in even greater increase in population numbers.

Hopfenberg and Pimentel (2001) pointed out that the perceived need to increase food production to feed a growing population is a misperception, a denial of the physical reality of the space–time dimension. If people are starving at a given moment in time, increasing food production cannot help them. Are these starving people supposed to be waiting for sowing, growing, and reaping to be completed? Are they supposed to wait for surpluses to reach them? Without food they would die. In such circumstances, increasing food production for people who are starving is like tossing parachutes to people who have

already fallen out of the airplane—the produced food arrives too late. However, this does not mean human starvation is inevitable.

If this view of the human population is somehow correct, then human population dynamics are not biologically different in essence from the population dynamics of other species (Hopfenberg and Pimentel 2001). We do not find hoards of starving roaches, birds, squirrels, alligators, or chimpanzees in the absence of food as we do in many civilized human communities today, because these nonhuman species are not annually increasing their own production of food. Among tribal peoples in remote original habitats, we do not find people starving. Like nonhuman species, "primitive" human beings live within the carrying capacity of their environment. History is replete with examples of early humans and other ancestors not increasing their food production annually, but rather living successfully off the land for thousands of years as hunters and gatherers of food. Before the agricultural revolution and the production of more food than was needed for immediate survival, human numbers supposedly could not grow beyond their environment's physical capacity to sustain them because human population growth or decline is primarily a function of food availability (Hopfenberg 2003; Hopfenberg and Pimentel 2001).

Given its current scale and rate of growth, the human population worldwide has identifiable, potentially destructive ecological consequences. From this theoretical perspective, recent global human population growth can be understood as a primary causative factor of a range of phenomena including biodiversity loss and environmental degradation.

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Sources of Blood Lead in Children

In their article on seasonality and children's blood lead (BPb) levels, Laidlaw et al. (2005) stated that "lead-contaminated soil in and of itself may be the primary driving mechanism of child BPb poisoning in the urban environment." We believe that the data presented by Laidlaw et al. (2005) do not support this conclusion and that they misrepresent the many other studies of childhood lead poisoning, which support a more comprehensive, validated approach.

To support their "soil-only" hypothesis, Laidlaw et al. (2005) made three primary arguments: *a*) soil lead represents a large and available reservoir of environmental lead; *b*) resuspension of lead from contaminated soil followed by inhalation of airborne particulate matter < 10 μm in diameter (PM_{10}) and dust deposition on interior surfaces is the major source of lead exposure to children; and *c*) the major source of lead contaminated soil is fallout from the past use of tetraethyl lead in gasoline.

Laidlaw et al. (2005) did not cite the compelling body of scientific evidence demonstrating that deteriorated lead-based paint and the contaminated dust and soil it generates is highly correlated with BPb levels in children. These have been reviewed at length elsewhere (National Academy of Sciences 1993; Jacobs 1995; President's Task Force on Environmental Health Risks and Safety Risks to Children 2000). Indeed, Laidlaw et al. failed to recognize the enlightened statutory definition of the term "lead-based paint hazard," which includes not only deteriorated lead-based paint but also interior settled house dust and bare soil. Together, these constitute the principal exposure sources and pathways for most (but not all) children today (Residential Lead-Based Paint Hazard Reduction Act of 1992—Title X 1992). Furthermore, documented evidence shows that soil lead levels are highest in soil at the house drip line and greatly decrease farther away from the house, regardless of whether or not the house is in a rural area or city (Jacobs 1995).

Laidlaw et al. (2005) ignored confounding due to the coexistence of old, poorly maintained lead-painted housing and traffic congestion in urban areas. They failed to develop any rationale to exclude lead paint as a prominent source of lead exposure and should have included a measure of it in their models. Furthermore, they did not support their assumption that PM_{10} data can be used as a surrogate for airborne lead particulate. Laidlaw et al. should have used the more direct measures of airborne lead particulate levels, which are available from the U.S. Environmental Protection Agency's (EPA) National Ambient Air Quality program (U.S. EPA 2004), rather than the convoluted indirect measures of particulate matter < 10 μm in diameter (PM_{10}), soil moisture, and other variables.

Studies of the effectiveness of soil removal in urban residential areas without addressing deteriorated lead paint have demonstrated that the "soil-only" approach being recommended by Laidlaw et al. (2005) is of limited value (U.S. EPA 1996). Even in Superfund sites where old mining and smelter wastes have resulted in very high soil lead levels, efforts that do not also address deteriorated lead paint often are disappointing. Furthermore, in the largest and most recent study of lead-based paint hazard control (which addressed lead paint hazards in > 3,000 homes in a dozen jurisdictions), house dust lead levels remained below preintervention levels for at least 3 years following the intervention (National Center for Healthy Housing and University of Cincinnati 2004). In a smaller follow-up study, dust lead levels remained between 11% and 75% lower than baseline levels for 6 years following lead-based paint hazard intervention (Wilson J, Pivetz T, Ashley P, Jacobs D, Strauss W, Menkedick J, et al., unpublished data). If the contention of Laidlaw et al. (2005) is correct (i.e., that urban soil lead is being resuspended and deposited inside homes), dust lead levels should have increased after intervention in these studies. In fact, they did not. This directly contradicts the authors' conclusions.

Finally, Laidlaw et al. (2005) erroneously cited a pooled analysis (Lanphear et al. 1998), which they believe supports their view that soil and dust lead are the most significant predictors of children's BPb. In fact, the model used in that study also included paint lead and paint condition as variables. If the dust and soil lead terms are forced out of the model, paint lead becomes the most significant predictor, which is consistent with the now well-known pathway of paint to settled house dust and bare soil, to children's hands, to ingestion through hand-to-mouth contact. The pooled analysis (co-authored by D.E.J.) cannot be used to justify Laidlaw et al.'s "soil-only" approach.

The latest figures from the National Health and Nutrition Examination Survey indicate that the enormous disparity in the prevalence of BPb levels > 10 μg/dL once seen between African-American and white children has diminished greatly [Centers for Disease Control and Prevention (CDC) 2005]. Overall, the number of children in the United States with excessive BPb levels has declined from 890,000 in 1991–1994 to 310,000 in 1999–2002. Much of this is the result of federal, state, and local efforts to create a reservoir of lead-safe housing in communities at greatest risk. This success is tempered by recent evidence that a safe BPb level for children has not been demonstrated. The lack of a safe threshold reinforces the realization that to prevent the adverse health effects caused by lead exposure, we must exercise the wisdom to recognize and address the many

sources of lead in children's environments. The reality is too complicated and the cost of failure too devastating to reduce this to a one-source solution.

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Blood Lead in Children: Laidlaw et al. Respond

Our article (Laidlaw et al. 2005) is about seasonality of blood lead (BPb) and developing a predictive model using climatic variables. It is a new and unique finding about lead, marked particularly by the fact that it identifies diffuse soil lead as a significant component of lead sources in urban children. In the article, we argued that meteorologic factors can be robustly applied as a predictor for seasonal variations in children's BPb, which can be used as a potential tool for health care clinicians in the fight to eliminate lead poisoning in youth. We did not intend to review the literature on lead sources; a vast literature already exists of such studies. Suggesting that we propose the "soil-only hypothesis" completely misconstrues our work.

Brown and Jacobs fail to appreciate our argument that lead accumulation in soil is from a combination of lead-based paint, leaded-gasoline, and many other sources, but is clearly not from lead-based paint alone. They fail to understand the fact that soil normally contains very small amounts of lead, and research from many cities has shown that there has been an excessive accumulation of lead in inner-cities (Filippelli et al. 2005; Mielke 2005). We acknowledge that multiple exposure routes for lead exist for children and likely influence the observed seasonality trends in BPb levels (Laidlaw et al. 2005). We seek to assist with scientific understanding of how and why inner-city children are commonly excessively exposed to lead, and we seek a solution to that problem.

We are concerned that people working at agencies that should champion the reduction of lead exposure do not appreciate the fact that multiple sources of lead have accumulated in urban environments and that all major sources and reservoirs need full attention if we expect to meet the goals of Healthy People 2010 (2005). Our work suggests that, to fully address the childhood lead exposure problem in the United States, a paradigm shift is required that includes all major reservoirs of active lead dust.

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Validity of Anogenital Distance as a Marker of *in Utero* Phthalate Exposure

In their article in the August issue of *EHP*, Swan et al. (2005) purport to show that anogenital distance (AGD) in male infants is correlated with maternal phthalate exposure during pregnancy. The AGD has been shown to decrease in male newborn rats following maternal exposure to antiandrogens (Gray et al. 2001). However, little is known regarding AGD in humans, or about effects on AGD, if any, following *in utero* hormonal exposure. Furthermore, significant limitations in the study undermine the validity of the correlation reported by these authors. Some major considerations include the following.

All male infants evaluated in the study appeared normal (Swan et al. 2005). Therefore, there is no evidence for potential adverse effect in the test population. Because little is known about AGD in human infants and its variation, no conclusion can be drawn whether the reported values are normal or abnormal. The range of AGD values seen among study subjects likely represents typical biologic variation that would be expected to occur among normal study subjects.

The only available historical data on AGD in male human infants (Salazar-Martinez et al. 2004) used a different parameter for male infants (distance from anus to the base of the scrotum), which did not show a similar correlation with maternal phthalate exposure.

Swan et al. (2005) failed to take into account the phenotypes of the parents as a variable that would influence the AGD of the study subjects, much as other human anatomical parameters (i.e., height) would have a genetic component.

The study subjects varied widely in age, height, and weight. To compensate for this variability, Swan et al. (2005) defined a new parameter, which they termed the "anogenital index" (AGI), by dividing AGD by body weight. In the absence of validation, the significance of the AGI is not known, and variation cannot be assumed to be related to hormonal exposure. Swan et al. suggested that the AGI is proportional to the normal genital development of male infants, but they provided no supporting evidence. Also, much scatter can be seen in the plot of "AGI by boy's age" (Figure 1; Swan et al. 2005). Salazar-Martinez et al. (2004) found that, in male infants, AGD correlated best with length, not weight.

Per definition, the AGD represents a one-dimensional parameter of the human anatomy. In analogy to similar anatomic parameters (e.g., length of limbs, hands, or feet), the AGD is likely to be proportional to body length and not to body weight. Therefore, Swan et al.'s use of the (body weight-related) AGI in the study has little biologic plausibility and appears to be arbitrary.

Swan et al. (2005) did not normalize maternal phthalate urinary concentrations for urine volume. This leaves open the possibility that higher urinary phthalate concentrations in individuals may have been due to lower urinary volume rather that higher phthalate exposure, and casts doubt on the maternal exposure classification categories. Phthalate levels were based on only a single sample per individual, and fetal development at the time of urine sampling was not reported.

Numerous maternal factors (alcohol consumption, medication, profession, body mass) may affect fetal development. Although it is unknown what factors, if any, would influence AGD in human infants, in the absence of these data, confounding factors cannot be excluded.

The levels of phthalates Swan et al. (2005) reported in maternal urine samples are extremely low, and the corresponding exposures are many orders of magnitude lower than the exposures at which selected phthalates have been found to have adverse reproductive effects in rodents. For example, assuming excretion of 2 L of urine/day, the reported concentration of butyl benzyl phthalate corresponds to an exposure of approximately 60 µg/day, or 1 µg/kg/day for a woman weighing 60 kg. Butyl benzyl phthalate has been shown to have only slight, hormone-like effects in rats at doses of ≥ 100 mg/kg/day (Nagao et al. 2000), or ~ 100,000-fold higher than the levels seen by Swan et al. (2005). In the case of the metabolite monoethyl phthalate, the expo-sure level for the corresponding parent compound diethyl phthalate was on the order of 1,000,000-fold lower than a level found to have no adverse reproductive effects in rats (4,000 mg/kg/day, the highest dose tested) (Scientific Committee on Cosmetic Products and Non-food Products 2002). It is biologically and toxicologically inconceivable that such low levels of human exposure would produce the significant structural differences claimed by Swan et al. (2005).

In summary, the relevance of AGD as an end point of interest in humans is entirely speculative, and the correlation reported by Swan et al. (2005) is lacking in biologic plausibility and remains unproven.

The authors are employed by advocacy groups that represent the interests of the cosmetic, toiletry, and fragrance industry.

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Anogenital Distance and Phthalate Exposure: Swan et al. Respond

In their letter, McEwen and Renner raise several points that we would like to discuss.

First, because all infants in our study (Swan et al. 2005) appeared normal, McEwen and Renner infer that there is no evidence of an adverse effect. However, the absence of evidence of an effect in infancy does not preclude serious adverse effects in later life. For example, the genital cancers that were identified in young women, on average 19 years after their prenatal exposure to the drug diethylstilbestrol, were seen in females who had appeared to be completely normal until that time (Herbst et al. 1971). In this case, unlike that example, we do have some evidence of anatomical changes in young boys. Although anogenital distance (AGD) has rarely been used as a measure of androgen action in humans, our data suggest that shortened AGD reflects reduced androgen action *in utero*; AGD was correlated with the degree of testicular descent and penile volume, and children with smaller AGD tended to have smaller scrotums; these are all signs of reduced androgen action.

McEwen and Renner state that the range of AGD reported in our study (Swan et al. 2005) is likely to be representative of normal study subjects. In fact, this information is not yet available because this is the first population-based study that utilized this measurement. AGD has, however, been used in the diagnosis of medical conditions such as congenital adrenal hyperplasia, in which AGD in females is increased by excess androgen exposure (Callegari et al. 1987). AGD is also known to be sexually dimorphic in humans as well as rodents (Salazar-Martinez et al. 2004).

McEwen and Renner point out that one previous study [*n* = 42; (Salazar-Martinez et al. 2004)] used an alternative measure of AGD in human infants. However, as we indicated in our article (Swan et al. 2005), this alternative definition is less precise than the one we used and does not correspond to the measure of anogenital distance most frequently used in toxicologic studies of rodents. Our use of this measure of AGD emphasizes the correspondence between traditional toxicology studies and our study.

In our study (Swan et al. 2005) we did not have data that would allow us to consider parental phenotype (e.g. parental height or father's AGD), as McEwen and Renner suggest should be done. If AGD was affected by parental stature (through infant body size), this association should be controlled for by adjusting for body size. Moreover, in order for a phenotypic variable to explain the observed association, it too would have to be related to maternal phthalate levels. This, too, would be an interesting finding.

McEwen and Renner question the use of normalizing AGD by dividing by weight (AGI) at examination. We examined several alternative measures of body size and, as discussed in our article (Swan et al. 2005), AGI provided the best fit to the data (independent

of phthalates). Vanderbergh and Huggett (1995) found the same to be true in rodents. The fact that there was some variation of AGI with age is to be expected; not all 1-year-olds have the same length, either.

McEwen and Renner point out potential sources of "exposure misclassification" which, we agree, may have been present (and we stated so) (Swan et al. 2005). However, unless these sources of measurement error were related to AGD, their presence would lead to underestimates of the strength of the associations we presented.

We examined a number of potential confounders, such as maternal smoking and alcohol consumption; the prevalence of both was quite low (Swan et al. 2005). None affected results appreciably. Of course, the phantom "unmeasured confounder" always lurks in the wings of any observational study, can never be ruled out, and is a favorite of critics of epidemiologic studies. Any constructive suggestions for alternatives to observational studies would be appreciated; the only alternative we know of, randomizing pregnant women to receive phthalates (or not), hardly seems ethical.

Rodent studies test only one phthalate at a time. As we demonstrated (Swan et al. 2005), women were exposed to measurable levels of multiple phthalates, many known to be reproductively toxic. Until we have data on the toxicology of this complex mixture, we do not have the information to draw conclusions about the relative toxicity of these compounds in rodents versus humans. Furthermore, although doses in rodent studies of specific phthalates are high, effects have been demonstrated at lower doses used in recent studies (Lehmann et al.). Unfortunately no toxicologic study has yet examined effects of phthalates at environmental levels. Because we did find a significant association with phthalates at such levels, we can only conclude that environmental levels, however low, are associated with somatic alterations in humans.

Our study (Swan et al. 2005) is relatively small and must be replicated; subsequent studies will undoubtedly eliminate many of the sources of potential exposure and outcome misclassification. Nonetheless, in this first study of its kind, we set out to test the hypothesis, suggested by a large toxicologic literature (Gray et al. 2000), that prenatal phthalate exposure is associated with several measures in humans that reflect the antiandrogenic action of these chemicals. Using similar outcome measures to those utilized in these toxicologic studies, that is what we found.

The authors declare they have no competing financial interests.

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ERRATA

In the October articles "Children's Centers Study Kids and Chemicals" [Environ Health Perspect 113:A664–A668 (2005)] and "Are EDCs Blurring Issues of Gender?" [Environ Health Perspect 113:A670–A677 (2005)], photographs and their captions erroneously imply that plastic drink bottles contain *ortho*-phthalates. Plastic drink bottles sold in the United States are made from polyethylene terephthalate and do not contain *ortho*-phthalates. Also, at the end of the EDCs article, references are made to plastic wrap and Saran Wrap. For clarification, neither plastic wrap nor Saran Wrap contains *ortho*-phthalates. *EHP* regrets these errors.

EHP regrets the incorrect and unintentional inference in "Paving Paradise: The Peril of Impervious Surfaces" [Environ Health Perspect 113:A456–A462 (2005)] that coal tar pitch is used in the actual hot-mix asphalt used to pave roads. Coal tar pitch is instead used in many sealcoat formulations used atop asphalt pavement. Findings published in the 1 August 2005 issue of *Environmental Science & Technology* suggest, in fact, that coal tar-based parking lot sealant may be a major contributor to stream loads of polycyclic aromatic hydrocarbons, including many known carcinogens.

In Figure 1 of the article by Chen et al. [Environ Health Perspect 113:1723–1729 (2005)], the legend should have read (*A*) PM_{10}; (*B*) $PM_{2.5}$, instead of (*A*) $PM_{2.5}$; (*B*) PM_{10}.

In Figure 1 of the article by Tsan et al. [Environ Health Perspect 113:1784–1786 (2005)], the double bond between HN and boron was incorrect. The corrected figure appears below.