

Compounds in Personal Care Products

Introduction

The widespread rise in the use of personal care products among women and men has coincided with increasing rates of breast cancer, leaving some to wonder if there is a connection. Of greatest concern are the natural and synthetic chemicals included in these products that are known or suspected carcinogens and those that may alter the body's endocrine activity. Most women use personal care products on a daily basis over an extended period of time, often applying a liberal amount to the skin. While many argue that these products contain a "safe" level of compounds of concern, below the regulatory standards,¹ the health effects of chronic exposure in humans have not been well studied.

Recent research has shown that some compounds commonly used in cosmetic and personal care products can mimic or block the action of natural hormones, including estrogens.² Some experts hypothesize that exogenous carcinogens, tumor promoters, and endocrine disruptors – along with altered breast sensitivity to these exposures – contribute to increased breast cancer incidence,³⁻⁶ and that the widespread and extended use of personal care products provides a potential source of such exposures.

The U.S. Food and Drug Administration (FDA) only minimally regulates chemicals in cosmetics and personal care products.⁷ Industry funds the Cosmetics Ingredient Review Panel to oversee its members, but relatively little is known about the potential health effects of the 5,000 or so ingredients in personal care products.

Definitions and Sources of Exposure

Three classes of compounds that have received considerable public attention are parabens, phthalates, and organic solvents. While these compounds are quite common in personal care products, they are also often found in other commonly-used consumer products and may be ubiquitous in the environment, making it very difficult to distinguish between sources of exposure. Many of the compounds of concern are also not identified on personal care product labels. The FDA cosmetic labeling law excludes fragrance components (such as phthalates) in commercial products produced for and sold solely to professional salons.⁷ The latter exemption particularly affects the large number of women who work in salons and are exposed to such products daily.

The FDA is only able to regulate cosmetics after products are released to the marketplace. Although the FDA must prove the likelihood of harm in order to regulate cosmetic compounds, manufacturers are not required to report inert ingredients. Laboratory analyses of cosmetic products sold in California have found products that contain substances known to or likely to cause cancer and not identified as an ingredient on the product's label. California recently passed the California Safe Cosmetics Act. This new law requires cosmetics manufacturers to disclose to the California Department of Health Services (CDHS) any ingredients "identified as causing cancer or reproductive toxicity."⁸ CDHS is authorized to investigate the chemicals' health impacts, and plans to make information about the products' components available to the public and

researchers. Whether the mandated reporting of compounds such as phthalates and benzene will lead manufacturers to reformulate their products remains to be seen. Regardless, many of these compounds are likely to remain in the environment at measurable levels.

Parabens, phthalates, and organic solvents are the three main chemical classes that will be discussed here. Other compounds of concern – including placenta/estrogens; plant oils; phenols found in UV filters (sunscreens), toothpaste, and antibacterial hand soaps; musks; and nanoparticles will also be addressed.

Parabens: Because of their antimicrobial and preservative properties, parabens have been used for 50 years to extend the shelf life of cosmetics, food, and other consumer products. Animal studies have shown that parabens are quickly absorbed from the gastrointestinal tract and from the blood, and the glucuronide conjugated form is excreted in urine.⁹⁻¹¹ Studies have also shown that parabens can be absorbed rapidly through the skin.¹¹⁻¹³ The six most commonly used parabens (methyl-, ethyl-, n-propyl-, isobutyl-, n-butyl-paraben and benzyl-paraben) have all been shown to have endocrine-disrupting properties – with weak estrogenic effects.¹¹ Substantial literature reviews have recently been conducted on these components of personal care products.^{14, 15}

Phthalates: As a principal component of polyvinyl chloride (PVC) products, building materials, pesticides, and personal care products, phthalates are used to render PVC softer and more flexible and to extend the scent stability in fragrances, cosmetics, and shampoos. Although phthalates are not persistent, they can be detected

in the blood or urine of nearly everyone because exposures are ubiquitous and frequent. These compounds have also been found in breast milk,¹⁶ but do not bioaccumulate in humans; they tend to be excreted through the urine and feces.^{17, 18}

The most widely used phthalates are di (2-ethylhexyl) phthalate (DEHP), di-isodecyl phthalate (DIDP), dibutyl phthalate (DBP), diethyl phthalate (DEP) and di-isononyl phthalate (DINP). The first of these is common in fragrances, but primarily used in plastics (see also Section I, Chapter B.9, Polyvinyl Chloride). DBP, DEP and butyl benzyl phthalate (BBP) are among the most commonly found in personal care products, including nail polishes, perfumes, soaps, lotions, and moisturizers^{19, 20} where they can reach up to 20 percent of the product volume.²¹

Phthalates may be absorbed through the skin when using personal care products; inhaled in household dust contaminated with phthalates from personal care products, vinyl flooring, shower curtains, adhesives, plastic toys, clothing, and building materials; or ingested eating food with phthalates from flavorings or leached from plastic wrap and containers. Exposures may also occur from medical treatment that uses equipment made with certain plastics, or from living near a facility that produces phthalates.²²

The relevance of exposure via personal care products has been demonstrated by the relationship between self-reported product use and levels of MEP, a urinary metabolite of DEP.²³ MEP levels are also higher among African Americans and among women.²⁴

Although there are conflicting published reports of estrogenic activity for phthalates in vitro, most studies demonstrate that their primary activity is anti-androgenic and that they may also affect enzyme activity.^{25,26} In vitro studies have shown that one phthalate, DEHP, is associated with the dose-dependent suppression of aromatase and has the ability to activate peroxisome proliferator-activated receptors (PPARs), possibly through receptor-mediated signaling.²⁷

Solvents: These chemical compounds are capable of dissolving, extracting, or dispersing/ suspending other substances. They are widely used and can enter the human body by ingestion, inhalation, and skin absorption. Exposure can occur through ingestion of polluted water sources or inhalation from working with or near solvents. Dermal absorption can be significant when the solvents are applied to or come into direct contact with the skin.

Solvents are used in the manufacturing of and can be a primary component of personal care products, including shampoo and hair styling products, perfumes, cosmetics, and nail products. They are used to extract and deliver other ingredients, create desired consistency, and extend color. While many are of low toxicity, solvents of some concern include:

Acetone (in nail polish and remover) is a suspected mutagen, but has not been classified for carcinogenicity. Breathing moderate-to-high levels for short periods of time can cause a shortening of the menstrual cycle in women, among other health effects.²⁸

Ethanol (in perfume, facial cleansers and moisturizers, and mouthwash) is readily absorbed, but in relatively low quantities from these products. It is generally not ingested in the quantities that link alcohol consumption with breast cancer.²⁹ Inhalation of ethanol is more associated with its use as a fuel and is addressed in Section I, Chapter B.1 of this report, Air Pollutants, Fuels, and Additives.

Ethylene glycol (in facial, acne, and hair treatments) may contain toxic impurities or contaminants, and there is limited evidence of reproductive or developmental toxicity.

Triethanolamine or TEA (in soaps, lotions, facial cleansers and treatments, perfume, hair and acne treatments, eye makeup and remover, antiperspirants, and baby products) and the less common Diethanolamine or DEA (in mascara, sunscreen, and body wash) are amines. If combined with nitrosating agents on the skin or in the body, amines can form carcinogenic nitrosamines. TEA is also a suspected endocrine disrupter.³⁰

Toluene (in nail polishes and treatments) is a possible human reproductive and developmental toxicant. Toluene is not classifiable as to carcinogenicity to humans according to the International Agency for Research on Cancer (IARC), but is often contaminated with small amounts of benzene. Toluene may also have endocrine-disrupting effects.³¹

Methylene chloride has been a common component of nail products. While it was used at low levels, many consumers and, especially, workers were exposed over long periods of time.

This solvent, and its predecessor, benzene, have been measured in human breast milk and linked to increased incidence of mammary gland tumors in rats and/or mice.³²

Other solvents, including benzene and methylene chloride, are addressed in Section I, Chapters B.1, Air Pollutants, Fuels, and Additives, and B.5, Solvents and Industrial Chemicals.

Other Personal Care Product Exposures: Other additives to personal care products are also of concern. Hair products that contain *placenta and estrogens* are hormonally active. These products are heavily marketed to African Americans to induce hair growth.³³ At least one study reports use by a majority of African Americans, including more than half of their young children.³⁴ Hair products containing placenta and estrogens are suspected of affecting the hormonal system, including altering the timing of puberty in girls.³⁵ Repeated topical use of personal care products with *natural plant oils, particularly lavender and tea tree*, has been associated with breast development in males as young as age four.³⁶ Growth receded after product use ended, and in vitro studies in human cell lines indicated that these oils were both weakly estrogenic and anti-androgenic.

Ultraviolet (UV) filters are extensively used in sunscreens and to promote product stability in other personal care products at concentrations exceeding 10 percent.³⁷

Several of these compounds appear to be estrogenic or anti-androgenic. In particular, benzophenone-3 (BP-3), homosalate (HMS), octyl-dimethyl-PABA (OD-PABA),

octyl-methoxycinnamate (OMC) and 4-methylbenzylidene camphor (4-MBC) have been shown to have estrogenic effects on cultured human breast cancer cells (they stimulated MCF-7 cell proliferation); more evidence of these compounds' estrogenic effects comes from in vivo experiments with rats.^{38, 39}

One of the most common sunscreen chemicals, 4-MBC, has exhibited the highest in vivo activity.³⁸ In water-dwelling animals, 4-MBC has been shown to cause potential change to the physiological and developmental processes mediated by estrogen receptor signaling mechanisms.⁴⁰ Due to concern for protecting skin from aging and skin cancer, use of such products has increased. These products are lipophilic and appear to be bioaccumulating in aquatic environments and fish.⁴⁰ While the major route of exposure for humans is likely direct dermal application, there is also likely some exposure through fish or other food consumption.⁴¹ At least one UV filter, BP-3, is easily absorbed through ingestion and has been detected in human urine and breast milk.³⁷ Another UV filter, octyl-methoxycinnamate or OMC, has also been detected in breast milk.

These and other UV filters, including 4-methylbenzylidene camphor or 4-MBC, have been increasingly studied over the past ten years. The limited evidence to date suggests that BP-3, 4-MBC, and several other of these compounds are estrogenic, anti-androgenic and anti-progestogenic.⁴² OMC was a weak estrogen alpha agonist but a strong progesterone antagonist. 3-BC and 4-MBC have both been shown to stimulate MCF-7 cell proliferation, and the latter

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has been linked to uterotrophy in rats.^{38, 39, 41} After daily application on humans, UV filters were measured in urine, but did not appear to affect levels of endogenous reproductive hormones in young men or post-menopausal women.⁴³

Musks are another compound of concern about which relatively little is known. They are used in almost all scented products, including perfumes, cosmetics, and even laundry detergents, and are found in all aquatic environments and in fish, where they are persistent.⁴⁴ Various musk compounds have been detected in human adipose tissue and breast milk.⁴⁵ Like UV filters, many of the musk compounds have been identified by in vitro and in vivo tests as hormonally active. Some appeared to be weakly estrogenic in vitro but were

not estrogenic in an assay using human MCF-7 cells.⁴⁵ Two polycyclic musks appear to be anti-estrogenic at high levels, and anti-progestogenic at very low levels.⁴²

The following table is a general summary of many of the compounds discussed above in relation to endocrine disruption, carcinogenicity, and disposition of the compounds in body fluids and tissues. Information about phthalates exposure from other than personal care products can be found in Section I, Chapter B.9, Exposures from Polyvinyl Chloride. Solvents are addressed elsewhere; ethanol in Section I, Chapter B.1, Air Pollutants, Fuels, and Additives and all others in Section I, Chapter B.5, Solvents and Industrial Chemicals.

Table 1. Select chemical constituents of personal care products and their link to endocrine disruption and cancer.

Compounds	Source	Mechanism(s) of Concern	Human/Animal Evidence
Parabens	Preservatives in cosmetics, food, and pharmaceuticals	Estrogen agonists	Measured in human milk and human breast tumors
Phthalates	Plasticizers, nail and hair care products	Estrogen agonists Androgenic antagonist Aromatase suppressor	Measured in human milk; animal studies indicate link with mammary carcinogenesis; adverse reproductive and development effects in animals; altered hormone levels
Solvents	Nail care products		
Benzene and Methylene chloride	Artificial nail products	Possible carcinogens	Measured in human milk; increased incidence of mammary gland tumors in rats and/or mice
Toluene	Nail polish	Endocrine disrupting effects	Measured in human milk
Acetone	Nail polish remover	Suspected mutagen	Affects menstrual cycle length
Other			
UV Filters (4-MBC, BP-3, OMC)	Sunscreen and cosmetics	Estrogen agonists Androgen and progesterone antagonists	Measured in human milk and urine MCF-7 cell proliferation, uterotrophic in rats
Musk	Fragrance in perfume, cosmetics, detergents	Estrogen antagonists Androgen and progesterone antagonists Potentially carcinogenic (non-genotoxic)	Measured in human milk, adipose tissue, and blood
Estrogen/placenta	Hair products marketed to African Americans	Earlier onset of puberty in African American girls	None

Nanoparticles: One overriding area of controversy is the use of nanoparticles in personal care products. These microscopic particles are added to consumer products to enhance skin penetration and to extend component stability. Conflicting evidence has been presented on skin penetration. There is evidence that they can penetrate broken or flexed skin and pass into the lymphatic system and regional lymph nodes, then potentially into the

circulatory system.⁴⁶ There is concern that some nano-sized substances may be toxic to human tissue and cell cultures, resulting in adverse health outcomes. While an industry study of titanium dioxide and zinc oxide nanoparticles found that the weight of the evidence shows they pose no threat to human health, they advised caution in using nano-sized particles of compounds that are able to penetrate the skin and/or have inherently toxic constituents.⁴⁷ There is still very little known

about potential exposure or about the deposition, translocation, and biopersistence of the myriad nanoparticles that are being used in personal care products and elsewhere, and new methods may be needed to identify potential risks.⁴⁸

Critical Review of Literature

Parabens: The use of personal care products has been implicated as a risk factor for breast cancer among women, particularly in the western countries where they are heavily used. One controversial hypothesis is that the estrogenic ingredients in underarm cosmetics (mainly deodorants and antiperspirants) have contributed to the rising breast cancer incidence in women over the recent decades.⁴⁹ Darbre called for more research into this potential link, given that: 1) underarm cosmetics are frequently and repetitively applied to and left on an area directly adjacent to the breast; 2) a large population is exposed due to widespread use, including higher-risk subgroups such as young adults; 3) personal care products contain compounds that are endocrine disruptors (e.g. parabens); and 4) there is suggestive evidence of intact paraben esters in breast tumor tissues, indicating a non-oral exposure route.¹⁴

While several chemical culprits were listed in the hypothesis (including aluminum salts and triclosans), parabens have received the most attention, mainly because of their estrogenic properties.⁴⁹ Parabens have been shown to have estrogenic effects in assay systems, both in vitro in human MCF-7 and ZR-75-I breast cancer cell lines⁵⁰⁻⁵² and in vivo in rodent uterotrophic assays.⁵²⁻⁵⁴ Parabens have also been shown to be dermally absorbed in animal and human studies,^{13, 55} lending further support to the hypothesis that

parabens from underarm cosmetics are absorbed through the skin. Conversely, some argue that parabens are only weakly estrogenic and that exposure occurs only at doses lower than those required for effect,^{15, 56} and, thus, that parabens are unlikely to cause any health effects. Proponents counter that no human health studies have examined chronic effects of low-level exposures to parabens to safely claim no adverse effect. Accordingly, the role of parabens and personal care products in breast cancer etiology should not be dismissed, particularly given their estrogenic activity.^{14, 57}

Other suggestive human evidence includes the relatively high proportion of carcinomas arising in the upper outer quadrant of the breasts, which is local to where the cosmetics are applied.⁵² A recent descriptive study in Nottingham using core breast biopsies, however, reported that the proportion of malignant to non-malignant histological findings between the four quadrants and the retroareolar region were not significantly different. While the results were not sufficient to refute the hypothesis of underarm cosmetics and rising breast cancer incidence, the author suggested that the trend for the high proportion of carcinomas in this area may be a reflection of the greater amount of breast tissue in this quadrant, and less likely a result of the personal care products used in that local area.⁵⁸

The epidemiologic data examining the relationship is also scant. To date, only two recent studies have attempted to address this question. A population-based case control breast cancer study found no difference in risk between women who used antiperspirants and those who used deodorants in

an analysis limited to women who also shaved their underarms.⁵⁹ Since both types of products may contain parabens, this study does not clarify the role of parabens, though it weighs against the hypothesis that blocking perspiration increases risk. Because use of underarm products is so common in the U.S., it would be difficult or impossible to assess risks in an epidemiologic study here because of the lack of unexposed women. A case-based study of breast cancer patients found that increased frequency of antiperspirant/deodorant usage and earlier age at onset of use was associated with an earlier age of breast cancer diagnosis.⁶⁰ While this study asked about age at menarche, it did not appear to control for the age of puberty onset. Some girls develop apocrine glands, those responsible for adult body odor, before their breasts and others develop breasts first and pubic hair and apocrine glands second. Pubertal timing would affect the relative sensitivity of breast tissue to exposure to the deodorant components during the crucial period of breast development.

Phthalates: In a report issued by the Centers for Disease Control and Prevention (CDC) in 2000, researchers found significant levels of seven phthalate monoesters and their metabolites in urinary samples from a reference population of 289 adult humans.¹⁷ While women of childbearing age in that study had higher levels of one phthalate, larger samples did not see a difference from children or older women.²⁴ Additionally, phthalates have been measured in human milk, implying their presence and availability to breast tissues.¹⁶

The findings of phthalates and their metabolites in urine and breast milk do not explain their origins, since these compounds are ubiquitous in the environment. However, the findings that women had higher levels of phthalates than did men suggests that women's personal care products may be a potential source. A smaller Korean study estimated that women's daily exposures to DEHP (41.7 µg/kg) was much higher than children's (male 9.9 µg/kg, female 17.8 µg/kg) and exceeded the European Union tolerable daily intake of 37 µg/kg, suggesting a significant difference in exposure.⁶¹ Childhood exposures are still of interest for future research. In a pilot study of six- to eight-year-old girls by the Breast Cancer and the Environment Research Centers, 94 percent had intermediate levels of concentrations of 9 out of 10 phthalate metabolites, with some significant racial differences.¹⁹

Although there is some evidence of reproductive and developmental effects from phthalates, no epidemiologic studies have been undertaken to examine the relationship between phthalates and breast cancer.⁶² Furthermore, animal studies have not considered the effects of phthalate monoesters on mammary gland development or pubertal timing in the female. Concern about a possible link between phthalates and breast cancer exists, however, because of phthalates' controversial in vitro estrogenic properties^{51, 63} and because they can act as endocrine-disrupting chemicals.^{6, 64-66} These endocrine disruptors can potentially affect breast cancer through promotional mechanisms, by affecting mammary gland development and the receptor populations normally expressed, or by responding to other carcinogens.⁶ Animal studies have reported suggestive evidence for the

protective effect of phthalates on the various stages of mammary carcinogenesis.⁶³ In contrast, *in vitro* studies reported that exposure to pharmacological levels of phthalate diesters can increase the proliferation of MCF-7 breast cancer cells.⁶⁴⁻⁶⁷ However, these studies do not agree on the concentrations of these compounds needed to stimulate cell proliferation of estrogen-receptor effects. These findings underscore the need to further explore the role of phthalates in the etiology of breast cancer, particularly given their ubiquitous presence in the environment and the significant body burden levels of these agents in the general population.

In the absence of clear evidence from human health studies, breast cancer advocacy groups and environmental organizations have taken a precautionary principle approach to phthalates. In 2005, U.S. Assembly Bill 908 proposed to ban dibutyl phthalate (DBP) and diethylhexyl phthalate (DEHP) from personal care products. The ability of cosmetic manufacturers to reformulate products to be phthalate-free, in order to comply with the European Union ban on DBP and DEHP, indicates that alternatives exist. However, U.S. legislators concluded that the current scientific evidence was inadequate to prove a public health risk. More and better evidence is needed to counter the strong industry lobbying on this issue.

Solvents: Several hypotheses have supported the biological plausibility of organic solvents causing breast cancer. One theory is that the estrogenic properties of halogenated hydrocarbons may be linked to breast cancer etiology.⁶⁸ Another theory is based on the lipophilic properties of organic

solvents, which allow them to pass more slowly from alveolar air to blood. Once in the blood, organic solvents can easily be transferred to the fat tissues.⁶⁹ This theory suggests that since organic solvents are lipophilic, they can migrate to the adipose tissue in the breast and can be stored there for significant amounts of time, where they can thereby initiate or promote carcinogenesis through genotoxic or related mechanisms.⁶⁹

Once organic solvents are in fatty tissue, they can be metabolized and expressed in human milk.⁷⁰ Biomonitoring studies have detected significant levels of solvents in breast milk, including benzene, methylene chloride, and toluene.^{69, 71-73} Breast milk levels of solvents may be higher than blood levels partly because breast fat does not eliminate solvents as quickly as does blood;⁶⁹ thus, their presence in breast milk indicates their bioavailability to breast tissue, possibly from a much earlier exposure.

Despite the suspected carcinogenicity of organic solvents in cosmetic products, a dearth of information exists on human health effects. A few occupational studies have reported a positive relationship between solvents and breast cancer among solvent-exposed workers⁷⁴⁻⁷⁶ but only one has been specific to solvents in cosmetic products. The California Occupational Mortality Study (COMS), a statewide population-based study that evaluated mortality data from 1979–1981 for different workforces compared to the general population, found significantly elevated breast cancer mortality rates – nearly two-fold – for cosmetologists, even after adjusting for smoking, alcohol, and SES.⁷⁷ Unfortunately, this mortality study did not specifically examine the relationship

between solvents and breast cancer; thus, the question about the role of organic solvents in breast cancer development still remains.

Health concerns have been particularly pronounced for hair and nail care service workers. Hair and nail services involve frequent and intense use of volatile chemicals, including organic solvents, which may present a health threat to the workers, consumers, and neighborhood residents. Of particular concern are the workers themselves, who have daily exposures to these agents over an extended period of time. The cosmetology industry in California is the largest professional licensee population of any industry or profession in the country, with nearly 400,000 licensees, including 206,000 cosmetologists and 83,500 manicurists.⁷⁸ The size and racial/ethnic composition of the workforce has also changed dramatically in the last few decades, notably, with a large composition of Vietnamese female immigrants working in this sector.⁷⁹ This demographic shift suggests a different set of risk factors for breast cancer (including genetic susceptibility and historical exposures) in this workforce and future studies should take these changes into account.

Other Personal Care Product Components: UV Filters: A single human study was identified related to UV filters. Janjua et al. found that young men and post-menopausal women who applied a combination of three sunscreen agents (BP-3, OMC and 4-MBC) in high concentrations (maximum to twice the maximum permitted) to their entire bodies daily had detectable plasma and urine levels of these sunscreen compounds.⁴³ The researchers found only minimal to no effect on

serum concentrations of reproductive hormones in either sex. This study suggests that there was substantial skin penetration, systematic uptake, and urinary excretion of the three sunscreen compounds, yet the compounds did not appear to have any influence on the levels of endogenous reproductive hormones in young men or post-menopausal women.

Estrogen/placenta: Several studies have been conducted on hair products containing estrogen/placenta. There is evidence that girls in the U.S. were starting puberty at an earlier age, with breast and pubic hair development appearing on average one year earlier in white girls and two years earlier in African American girls.⁸⁰ Obesity was found to be an important contributing factor for the overall earlier onset of puberty, but it did not account for all the interracial difference in onset of breast development; additional factors are needed to explain the higher prevalence of early puberty in African American girls compared to white girls.⁸¹

Some preliminary evidence points to the more frequent use of hormone-containing hair products among African Americans as the culprit for a higher prevalence of sexual precocity in this population. A survey of the frequency of use of certain hair-treatment products containing hormones or placenta among different racial groups attending the pediatric clinics of military treatment facilities reported that 55.5 percent of African American parents used these products on their children, compared to 6.9 percent among white parents.³⁴ A study examining advertising for women's personal care products from 1950 through 1994 in widely-read, long-lived

magazines reported that hair products containing hormones or placenta were much more likely to be advertised in magazines with a predominantly African American readership (e.g. *Essence* and *Ebony*), compared to magazines such as *Mademoiselle* and *Ladies' Home Journal*.² These findings suggest that African American women and girls are likely to have different patterns of use of personal care products, particularly hair products that may contain hormones or placenta.

Two case series suggested that exogenous hormones in hair products may be associated with early pubertal development in African American girls. In 1998, Tiwary reported that four African American girls, aged 14 to 93 months, developed breast or pubic hair two to 24 months after the parents started using estrogen- or placenta-containing hair products on them. These symptoms decreased after the discontinuation of such products in three of the four patients.³⁵ Another study reviewed records of children referred for evaluation of sexual precocity and found that the eight African American children with symptoms of early puberty were using products containing exogenous hormones.⁸² With so many other suspect substances for earlier puberty and with the scant literature on the relationship between estrogen-containing hair products and earlier puberty onset, further studies are needed. However, if there is a causal relationship, this may have implications for breast cancer risks among African American women, particularly since breast cancer rates are higher for pre-menopausal African American women compared to pre-menopausal white women. A more recent study found no association between hair relaxer use and risk of breast cancer.⁸³

Summary and Future Directions for Research

Parabens: Given the significant role of estrogen and endocrine disruptors in breast cancer, widespread use of cosmetic products among a potentially vulnerable population of young women, and mildly suggestive toxicological data, it is logical to include parabens in the research agenda to explore etiologic factors that contribute to this disease. Future research should combine both toxicologic and epidemiologic methods, with more attention focused on exposure assessment, particularly historical exposures, given the long latency period for breast cancer. In summary, the hypothesis remains controversial and further research is needed to shed light on this question.

Phthalates: Despite the lack of human health studies, toxicologic evidence exists suggesting a possible link between phthalates and breast cancer. Cosmetic products have been shown to contain varying forms and amounts of phthalates and the presence of phthalates in urine and breast milk indicates that these compounds are bioavailable and remain in the body after environmental exposure. Future research is needed to examine the role of phthalates in mammary carcinogenesis, taking into account individual exposures levels and their sources of exposure in order to plan for future risk-reduction efforts. Since phthalates are widely used in the cosmetics industry, including in nail polish, hair products, fragrances, and skin creams, future research should include studies of hairdressers, nail care workers, perfume counter technicians, makeup artists, and other occupational groups who routinely handle many of these products.

Solvents: In summary, few human studies exist on the influence of organic solvents in cosmetic products on breast cancer, despite the mammary carcinogens widely used in these products. Because of the widespread use of potential mammary carcinogens in many nail and hair care products, organic solvents should become a high priority for the breast cancer research agenda. Future research should include studies of cosmetologists; particularly nail salon workers who have daily exposures to these volatile chemical compounds. These studies should focus on valid and reliable exposure assessment methods that take into account individual historical exposures. While biomonitoring methods exist to indicate recent exposure to some solvents, air monitoring may be more reflective of the current levels of exposures, which may differ greatly from past exposures, given the dramatic changes in this industry in recent decades. Air monitoring may also help distinguish the source of exposure, i.e. workplace exposure as opposed to second hand smoke at home or outdoor air pollution. Identifying the source of organic solvent exposure can help with interventions to reduce levels of exposure for both workers and consumers of cosmetics. Breast cancer research related to nail salon worker exposures may be particularly of interest, as this type of business did not exist 40 to 50 years ago, workers are often younger, and it could indicate if infant and young girls are at increased risk from using nail products.

UV Filters: Given the suggestive evidence of hormonal activity, further research is warranted into how these compounds act in humans and their role in breast cancer etiology. Greater attention

should be paid to 4-MBC because of its common use and higher in vivo effect.³⁸

Discussion: While there are some noticeable differences among parabens, phthalates, and solvents with respect to their chemical properties and their purpose in products, they share very common characteristics of potential concern – estrogenic properties, other hormonal effects, and absorption into breast tissues. Curiously, there have been no systematic research efforts to examine their effects in human populations that are vulnerable to such exposures. The lack of epidemiologic studies appears to be mainly due to study design limitations (i.e. difficulties in conducting exposure assessment) and minimal resources, rather than lack of a clear rationale for further exploring these environmental links. Finding a population that is not exposed to parabens, phthalates, or solvents would be extremely difficult; therefore future studies may be best focused on in vitro and animal models, and longitudinal biomonitoring to compare relatively higher and lower exposures, such as the BCERC study. Reliance solely on animal studies has been criticized as providing insufficient evidence. However, evidence from these studies that indicates early-life exposures stimulate effect, when adult exposures do not, should be heeded.

Industry scientists are working on estimating exposure to personal care products as part of their safety assessments.⁸⁴ Most effective would be to require more extensive testing before these products are marketed, similar to the system used for drugs. Such testing would be useful not just for synthetic compounds, but also for natural components of personal care products. For

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example, tea tree and lavender oils were recently suspected of causing breast growth in young boys and found to have estrogenic and anti-androgenic activity in human cell lines.³⁶

Different interest groups, including industry and nonprofit organizations, have sought to influence the regulation of compounds in personal care products. Public policy appears to have been driven more by interest groups than by human health evidence, especially given the lack of human studies in this area. Often, the lack of scientific endeavors has been spun as a lack of supporting evidence for the link between the compounds and breast cancer, a misinterpretation that needs to be clarified with policy makers. Given that research has been trailing policy changes, it is imperative that more resources be dedicated to conducting human health studies on this issue to inform sound public policy and better serve the public's interest.

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