Pervasive Parabens:

Their Destructive Role in Male and Female Health, Obesity, and Mitochondrial Function

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In the modern world, the regimens we develop for our patients must be employed in a setting where individuals come into contact with pervasive endocrine-disrupting chemicals that can negate the effects of strategies designed to optimize health. Our patients are constantly exposed to an alarming number of these toxic environmental chemicals, but I will confine the discussion in this article to a group of chemicals known as parabens (methylparaben, ethylparaben, propylparaben, and butylparaben), antimicrobial preservatives used in many personal care, cosmetic, and pharmaceutical products including body lotion, shampoos, soaps, conditioners, make-up, toothpaste, deodorant, and perfume. Testing patients for their paraben and other toxic burdens is paramount when identifying obstacles to enhanced wellness.

The use of lotions, cosmetics, cologne/perfume, nail polish, suntan lotion, or hair gel is associated with a 28% to 80% higher level of parabens and another toxic group of chemicals known as phthalates compared to women not using these products.[1] Women who use lotion have urinary butylparaben and propylparaben levels two to three times higher compared with non-users.[1] Furthermore, regular use of perfume can result in methylparaben levels that are 45% more compared with women who don't use cologne.[1] On account of the increased use of personal care products, parabens have been found in 98% to 100% of pregnant women.[2]

Parabens are also observed in wastewater, rivers, soil, and household dust.[3] Their presence in some food packaging allows them to seep into food and beverages.[4] In a study of Belgium subjects, depending on the type of paraben, this chemical was detected in urine samples from 83.1% to 100% of participants.[4]

Parabens are known to exert weak estrogenic activity and their toxic effects may be due to not only this property but also via other mechanisms of action. No matter how healthy patients eat or how much time they spend exercising, these health-promoting measures won't matter if they do nothing to minimize their exposure to—and the effects of—parabens.

Parabens and Melanoma

The incidence of cutaneous malignant melanomas (CMM) in young adults has increased over the last several decades.[5,6] CMM occurs primarily in women ages 15 to 34.[4] Although genetic susceptibility or ultraviolet light exposure may play a role, science indicates that pesticides or endocrine-disrupting chemicals may also be involved in the pathophysiology of the disease.[4] Higher exposure to parabens has been associated with the increasing incidence of CMM.[7]

Parabens act on estrogen receptors and these same receptors are expressed in melanoma cells.[4,8] By inducing oxidative stress, methylparaben also exacerbates skin damage caused by ultraviolet radiation.[9] The increased exposure of parabens in women, who typically use cosmetics, may explain the higher incidence of CMM in this population.[4]

Breast Cancer

A number of in vitro studies have established an association between exposure to parabens and breast cancer development. Combinations of parabens at levels measured in human breast tissue stimulate proliferation of MCF-7 human breast cancer cells.[10] Furthermore, propylparaben has been shown to suppress apoptosis in breast cancer cells.[11]

In another study, researchers exposed MCF-7 breast cancer cells and a patient-derived xenograft (estrogen receptor positive) to physiological levels of methylparaben.[12] Exposure to methylparaben resulted in increased tumor size of MCF-7 xenografts and estrogen receptor positive patient-derived xenografts tumors. In vitro, methylparaben failed to increase MCF-7 cell proliferation or activate estrogen-responsive genes.[12] Therefore, methylparaben enhanced activity of tumor-initiating cells possibly through a mechanism independent of the estrogen receptor.

In humans, there is cross-talk between estrogen receptor α (ERα) and the human epidermal growth factor receptor (HER) family. This cross-talk can increase the potency of parabens. This was demonstrated in a cell-culture study where butylparaben combined with a HER ligand heregulin (HRG) resulted in a synergistic proliferation of HER2-positive human BT-474 breast cancer cells compared with butylparaben alone.[13] This synergistic action was accomplished through the ERα. According to the study authors, "Parabens might be active at exposure levels not previously considered toxicologically relevant from studies testing their effects in isolation."

Few human studies investigated the effects of parabens on breast cancer. One review of the risk of breast cancer in African American women who use hair products including root stimulator, hair oil, and perm/relaxer not containing lye, found an association between use of these products, many of which contained parabens, and increased breast cancer risk.[14]

Parabens have been found in human breast tumors.[15] Breast cancer occurs more often in the upper outer quadrant of the breast, in the axilla area. Levels of propylparaben were markedly greater in the axilla compared with the mid and medial regions.[16]

Human studies investigating whether deodorant or antiperspirants, which contain parabens, are associated with increased breast cancer risk have produced conflicting results. Two studies found no association between breast cancer and deodorant use.[17,18] However, McGrath observed that increased frequency and earlier onset of antiperspirant/deodorant use combined with underarm shaving correlated with receiving a breast cancer diagnosis at an earlier age.[19]

Other Effects on Male and Female Health

Preliminary studies have detected parabens in human ovarian cancer tissues. Malignant ovarian tumor tissues had higher levels of parabens compared with benign tumor tissue samples.[20] Parabens also have an effect on the prostate. Oral exposure to methylparaben in male adult gerbils resulted in morphological changes in prostates including epithelial hyperplasia, increased cell proliferation, and a higher frequency of androgen-receptor-positive cells.[21]

The Effect of Parabens on Reproductive Health

As endocrine-disrupting, estrogen-mimicking chemicals, parabens can adversely affect the reproductive system. Human and animal studies indicate that these chemicals are linked to infertility. Higher exposure to parabens in women is associated with lower antral follicle counts,[22] an indicator of infertility. Greer and associates determined that the greatest chance of having a preterm birth occurred in pregnant women with the highest paraben levels.[23] Furthermore, infants conceived to these mothers had lower gestational age at birth, decreased birth weight, and shorter body length. In another study, Smarr and colleagues demonstrated that women with the highest urinary concentrations of methylparaben and ethylparaben had less children compared with women with lower concentrations of these chemicals.[24] One rodent study showed that oral exposure to methylparaben during pregnancy resulted in a larger litter size, but also increased offspring mortality.[25]

Prenatal exposure to parabens can have long-lasting consequences. Oral and subcutaneous exposure to butylparaben in pregnant animals leads to problems in the offspring including impaired social interactions, learning, and memory.[26] The social impairment resembled that seen when autism was induced in the rats.

Obesity

Parabens belong to a group of chemicals known as "obesogens," which can promote adipogenesis and lead to weight gain.[27] Because obesogens have a primarily lipophilic structure, their ability to increase fat deposition results in their own retention. This promotes obesity and also the retention of other lipophilic chemicals that have a greater range of toxic properties.[27] This could be one reason why obesity is a risk factor for cancer.

Animal and in vitro studies have presented evidence for parabens' role as an obesogen. Exposing mice to methylparaben after weaning increased adiposity and serum leptin levels, but butylparaben had no effect.[28] Parabens also enhance adipocyte differentiation in murine cells.[29]

Mitochondria-Damaging Effects

The detrimental effects of parabens may be in part explained by their impairment of mitochondrial function. For example, paraben-induced mitochondrial dysfunction in the testis is associated with male infertility.[30] A rat model of autism led researchers to propose that the means by which butylparaben may increase the risk of this disorder is through mitochondrial dysfunction and reduced production of energy carriers (AMP, ATP and AMP/ATP ratio).[31] In rat hepatocytes, propylparaben was the most toxic of all parabens tested and this toxicity was associated with depleted ATP levels via mitochondrial dysfunction of membrane potential and/or oxidative phosphorylation.[32]

Parabens and the Gut Microbiota

Evidence is emerging that parabens and other environmental chemicals may alter the composition of the gut microbiota. Hu and colleagues administered diethylphthalate, methylparaben, and triclosan alone and together to rats from birth to adulthood at doses similar to those which humans are exposed.[33] The researchers observed significant alterations in the overall bacterial composition in the adolescent rats. Specifically, there was an increase in the relative abundance for Bacteroidetes (Prevotella) and a decrease in the relative abundance of Firmicutes (Bacilli) in adolescent rats exposed to the chemicals from birth compared to controls. Surprisingly, the alterations in the gut microbiota disappeared by adulthood. More research is needed to fully elucidate the effects of parabens on the microbiota.

Paraben Avoidance

Reducing exposure to parabens is critical to avoid their potentially toxic effects. Urging patients to replace paraben-containing lotions, soaps, shampoos, toothpaste and other personal care items with paraben-free products is an important step. Recommending that they wash their hands before eating to eliminate any contact with parabens found in dust is another way to minimize exposure to these toxins.

Dietary Supplementation to Protect Against Parabens

The detrimental effects of parabens on the mitochondria suggest coenzyme Q10 may be employed to reduce the damage done by these toxins due to COQ10's well-known mitochondrial-protecting actions. It is also logical that supplementing with antioxidants will protect against oxidative damage induced by parabens.

Mouse studies and cell culture experiments indicate that ginger (Zingiber officinale) can reduce paraben-related damage. Asnani and Verma studied the effect of an orally administered aqueous extract of ginger (3 mg/animal/day) on lipid peroxidation caused by parabens in the liver of mice for 30 days.[34] Ginger significantly reduced paraben-induced lipid peroxidation and markedly improved activities of enzymatic (superoxide dismutase, glutathione peroxidase, catalase) and non-enzymatic (glutathione and ascorbic acid) antioxidants in the liver of mice, compared with the animals given only paraben. In a similar study, the same researchers found that ginger reduced the paraben-induced biochemical alterations in the liver and kidneys of mice.[35] In vitro studies conducted by the same scientists found that ginger acted as an antioxidant that inhibited lipid peroxidation caused by parabens and inhibited paraben-induced cytotoxicity.[36,37]

Conclusion

Our patients are exposed to many environmental threats to health, including a group of toxic chemicals known as parabens. These endocrine disrupters have been linked to melanoma, breast cancer, changes in ovarian and prostate tissue, reproductive problems, obesity, and autism. Parabens interfere with mitochondrial function and may alter the composition of the gut microbiota. Identifying and quantifying a given patients toxic burden prior to and after detoxification efforts allows the functional medicine provider to know how best to support the body nutritionally to best adhere to mandate to "do no harm". Therefore, for any health-supporting regimen to be effective, we must intelligently reduce paraben exposure and protect the body against their damaging effects.

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