Environmental Medicine Update

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What Affects Men's Hormones?

Many chemicals that we are exposed to through food, water, plastics, personal care products, and lifestyle choices can mimic and alter hormones in the body. These chemicals are called hormone-disrupting compounds and have been linked to reproductive and other health problems. Most of the science is focused on the health effects of these chemicals in women and children. But they also affect men and are starting to cause concern that men's reproductive and hormonal health is at risk. Here is review of some of the recent studies linking chemicals in the environment to hormonal changes in men.

Pesticides Block or Mimic Male Hormones

A recent study published in the journal *Environmental Health Perspectives* discovered that pesticides, some previously unknown to disrupt hormones, had antiandrogenic effects in men. Scientists at the University of London studied 37 pesticides for in vitro androgen receptor (AR) antagonism. Of these, 14 were previously reported to be AR antagonists, 4 were predicted AR antagonists, 6 were predicted to not be AR antagonists, and 13 had unknown activity. All 14 pesticides with previous evidence of AR antagonism were confirmed as antiandrogenic, and 9 previously untested pesticides were identified as antiandrogenic. They were: dimethomorph, fenhexamid, quinoxyfen, cyprodinil, λ-cyhalothrin, pyrimethanil, fludioxonil, azinphos-methyl, and pirimiphos-methyl. In addition, 7 compounds were classified as androgenic.[1]

Comment: This study is significant because it focuses on pesticides currently being used and found on fruits and vegetables. Past studies focused on pesticides that are no longer registered for use in the US and developed countries. In this study, 30 out of 37 pesticides tested altered male hormones. Most of the newly discovered hormone disruptors are applied to fruits and vegetables. Many of these had never been tested for hormone disruption activity. The researchers screened the pesticides using in vitro assays, which use human cells to check whether the pesticides activate or inhibit hormone receptors in cells. It is not known how these pesticides will behave in the human body at concentrations from consuming fruits and vegetables. The researchers strongly recommended that all pesticides in use today be screened to check if they block testosterone, which is critical to men's reproductive health and aging. This idea faces major opposition in the US from the pesticide industry. In the US, the Environmental Protection Agency is responsible for testing chemicals found in food and drinking water to see if they interfere with hormones. None of the newly discovered pesticides with hormonal activity is included in the EPA's testing program, which means that they are not currently screened and there are no plans to do so.

Bisphenol A Affects Men's Thyroid and Reproductive Hormones

One hundred sixty-seven men were recruited from an infertility clinic at Massachusetts General Hospital. Men aged 18 to 55 without postvasectomy status participated in the study. Bisphenol A (BPA) was measured in a single urine sample of the 167 men, and blood hormone levels were measured the same day. Seventy-five of the men submitted a second urine sample and 4 men a third sample for measurement of BPA. These were collected one week to two months after the original sample. Hormones tested for were testosterone (T), estradiol (E2), sex hormone binding globulin (SHBG), inhibin B, follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin, free T4, total T3, and TSH. A free androgen index (FAI) was calculated as the ratio of total testosterone to SHBG. Results of this study showed that in spot urine samples collected on the same day as blood samples, urinary BPA concentrations were inversely associated with serum levels of FSH, inhibin B, FSH:inhibin B ration, and E2:T ratio. When one or two urine samples were collected in the weeks or months following collection of the blood sample, then the inverse association involving BPA and FSH and inhibin B weakened. Inverse associations were also found between BPA and SHBG, FAI, estradiol and TSH. The results of this study indicate that BPA exposure may be associated with altered hormone levels in men.[2]

Comment: BPA has long been known to be a hormone-disrupting chemical and linked to many health conditions

in women, including infertility. The main way that we are exposed to BPA is through food and water. BPA can leach into food from the protective internal epoxy resin coatings of canned foods and from products such as polycarbonate plastic tableware, food storage containers, water bottles, and baby bottles.[3] This recent study looks at BPA and men's hormones. BPA was collected in the urine from men presenting to an infertility clinic in Massachusetts. Urine is a good measurement for BPA, since it is rapidly metabolized and excreted from the body after exposure. Nine men were excluded from the study because they were already taking medications that alter hormone levels, such as finasteride or Clomid and GnRH, testosterone, or prednisone. The study's finding that BPA is inversely associated with serum E2:T ratio is significant, since estradiol is produced through aromatization of testosterone. A reduction in the E2:T ratio is considered a marker for decreased aromatase activity. This had been shown in the past in animal studies but not humans. BPA is known to have antiandrogenic activity in a number of studies and is confirmed here in regard to its decrease in FAI, E2, and TSH. Of course, there are several limitations to this study, which the authors point out; but given the widespread exposure to BPA and its known adverse effects on hormones and reproductive health, steps should be taken to minimize or eliminate the general population's exposure.

Phthalates from Plastics Have Negative Effects on Men's Hormones and Fertility

A recent study soon to be released in the *Journal of Andrology* has linked several phthalate monoesters to changes in men's hormones. This study includes men from two large ongoing studies looking at the environmental links to health. One of these, the Study for Future Families (SFF) is a multicenter study of *pregnant* women and their male partners, conducted at prenatal clinics affiliated with university hospitals in five US cities between 1999 and 2005. The second study included men who were male *partners in infertile couples* seeking evaluation at the Vincent Memorial Obstetrics and Gynecology Service, Massachusetts General Hospital, between January 2000 and May 2004.

In both studies the men completed a questionnaire and gave urine, blood, and semen specimens. Information was collected on demographics, medical history, and lifestyle factors. Four hundred and twenty-five men in each study population provided urine and blood samples. Urinary phthalate metabolites were measured in men, along with serum hormone levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), testosterone (T), inhibin B, estradiol (E2), sex hormone-binding globulin (SHGB), and a free androgen index (FAI). Urinary concentrations of three metabolites of DEHP (mono-2-ethylhexyl phthalate [MEHP], mono-2-ethyl-5-hydroxyhexyl phthalate [MEHHP], and mono-2-ethyl-5-oxohexyl phthalate [MEOHP]) were inversely associated with the free androgen index (FAI) and calculated free testosterone (FT). Urinary concentrations of MEHHP and MEOHP were positively associated with SHBG, and MEHP was inversely associated with E2. No other phthalate metabolites were associated with serum hormones, consistent with results in each population. The study concludes that exposure to DEHP at environmental concentrations is associated with declines in free testosterone, both FAI and FT, and serum estradiol (E2). The other phthalate monoester metabolites examined (MEP, MBP, and MBzP) were not associated with any reproductive hormone changes.[4]

Comment: This is the first study to examine the associations between urinary concentrations of phthalate metabolites and reproductive hormone levels in a large study including both fertile men and male partners in infertile couples. This study suggests that DEHP has some antiandrogenic effects that alter male hormones and could affect fertility. Previous studies, including animal studies, have shown this same effect and proposed that DEHP is associated with reduced aromatase activity.[4] Although this study looks at a large cohort of men, one limitation is that the study population from infertility clinics is not representative of the general population. However, according to data from the most recent National Health and Nutrition Examination Survey (NHANES), metabolites of DEHP are in 99% of the general population.[5] DEHP is used in the production of polyvinyl chloride (PVC), and many men are exposed to it without being aware. DEHP migrates into food from plastics during processing and storage. It is in other products, including flooring, wall coverings, furniture, footwear, baggage, and packaging. Medical devices made of flexible PVC, such as IV bags and tubing, can leach the phthalate DEHP into patients.[3] It is possible for physicians to order IV tubing and bags free of phthalates, while men should try to make healthful lifestyle choices by minimizing the use of plastics and plastic products.

Summary

These three studies highlight the concern about chemicals in the environment and men's health. Men are exposed to bisphenol A and phthalates on a daily basis from the use of plastic beverage bottles, plastic storage containers, plastic wrap on food, and canned foods. Men are exposed to pesticides through consumption of conventional fruits and vegetables that contain pesticide residue. While these chemicals have long been known to cause hormone disruption in animals, research has also shown that they affect humans. In the past, scientists have focused on the health effects of these chemicals on women and children, including infants. These three recent articles highlight the emerging concern for men. While scientist continue to bicker and claim that more research needs to be done, and industry responsible for putting these chemicals into products insist that they are safe, the public is starting to demand that they be removed from the environment. Some states are taking regulatory action that the federal government has resisted doing. For example, seven states have banned BPA from consumer products sold within their borders. Learn more about these and other hormone disrupting chemicals in my book, *8 Weeks to Women's Wellness.*

Notes

1. Orton F et al. Widely used pesticides with previously unknown endocrine activity revealed as in vitro antiandrogens. *Environ Health Perspect.* 2011;119:794–800.
2. Meeker JD, Calafat AM, Hauser R. Urinary bisphenol-A concentrations in relation to serum thyroid and reproductive hormone levels in men from an infertility clinic. *Environ Sci Technol.* 2010;44(4):1458–1465.
3. Marchese M. *8 Weeks to Women's Wellness: The Detoxification Plan for Breast Cancer, Endometriosis, Infertility, and Other Women's Health conditions.* Petaluma, CA: Smart Publ.; 2011.
4. Mendiola J et al. Urinary concentrations of di(2-ethylhexyl) phthalate metabolites and serum reproductive hormones: Pooled analysis of fertile and infertile men. *J Androl.* Epub May 19, 2011.
5. Aylward LL, Hays S, Kirman C. *Urinary DEHP Metabolites and Food Fasting Time in NHANES.* Consumer Products Safety Commission. September 8, 2010. Accessed online July 25, 2011. http://www.cpsc.gov/about/cpsia/chap/urinaryDEHP.pdf.

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