Disinfection By-products and Bladder Cancer

Common Genetic Variants May Confer Increased Risk

Disinfection of the water supply is an important and cost-effective tool to reduce morbidity and mortality from a wide range of infectious diseases. However, the chemicals used to treat water also can produce potentially toxic compounds known as disinfection by-products (DBPs). A new study shows strong associations between DBP exposure and bladder cancer among individuals who carry inherited variants in three genes (*GSTT1*, *GSTZ1*, and *CYP2E1*) that code for key enzymes that metabolize DBPs [***EHP* 118(11):1545–1550; Cantor et al.**].

DBPs form when disinfectants (such as chlorine) react with organic matter that collects in water (such as algae or humic acids from decayed leaves). Most DBP exposure is due to ingestion of drinking water, although some DBPs can be inhaled or absorbed through the skin during bathing, showering, or swimming in a pool. Laboratory studies show that many DBPs are mutagenic or carcinogenic, but epidemiologic studies to date have revealed only a modest association between DBP exposure and cancer in humans.

In the present study, 595 men and 85 women newly diagnosed with bladder cancer were recruited from 18 hospitals in Spain and matched with controls (622 men and 92 women) who had been hospitalized with conditions thought to be unrelated to bladder cancer. The authors estimated DBP exposure since age 15 years by linking participants' residential histories with documented and estimated levels of trihalomethanes (THMs)—a DBP often used as a marker for total DBP exposure—in municipal water systems. Participants were genotyped for variations in *GSTT1*, *GSTZ1*, and *CYP2E1*.

Across the study population cancer risk nearly doubled between the highest and lowest levels of DBP exposure, and the association with DBP exposure was even stronger among participants who carried one of three variant genotypes. Smokers also had a higher risk (smoking is the most significant known risk factor for bladder cancer).

One of the genotypes appeared to increase the association between DBPs and bladder cancer codes for the active form of the enzyme glutathione transferase theta-1 (GSTT1), which metabolizes brominated THMs to mutagens. Another increases the activity of cytochrome P450 2E1 (CYP2E1), which catalyzes the primary oxidation of THMs. There is evidence the third genotype may reduce the activity of glutathione transferase zeta-1 (GSTZ1), which transforms haloacetic acids, another type of DBP, to less toxic compounds.

Among individuals who carried both of the *GSTT1* and *GSTZ1* genotypes noted above (28% of study participants), those with the highest DBP exposure were at a 1.5 times increased risk of bladder cancer compared with carriers with the lowest DBP exposure. These genotypes are relatively common, occurring jointly in more than 20% of the controls in the study population. The findings from this study therefore may have significant public health implications for cancer prevention.

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A Balanced Diet?

Selenium May Offset the Effects of Methylmercury on Cataract Development

Dietary exposure to mercury from fish has been posited as a risk factor for cataracts because some reports have suggested methylmercury accumulates in the lens of the eye. But selenium from other dietary sources may offset that damage, according to a study of communities in the Amazon basin [***EHP* 118(11):1584–1589; Lemire et al.**]. The findings, while preliminary, hint at potential public health measures in areas where methylmercury-contaminated fish are a significant part of people's diets.

With old age comes cataracts, particularly in latitudes like the Amazon, where higher ultraviolet radiation exposure and other environmental factors contribute to the clouding of the lenses in human eyes. And while surgical fixes exist for cataracts, people in isolated regions may not always have access to those options. Cataracts therefore are a major cause of blindness among older people in the Amazon.

The current study involved communities that eat fish from the Tapajós River, a tributary of the Amazon. People here have among the highest reported exposures to mercury in the world. Deforestation in the region leads to the release of natural inorganic mercury from soils into surface waters, where it is methylated and eventually ends up in fish.

Several hundred people voluntarily participated in the study, which entailed taking an overnight boat trip to a nearby city where participants gave blood samples and were examined by optometrists. In the end, 211 people over age 40 were included in the analysis. A third of them had age-related cataracts.

Low plasma selenium and high blood mercury each were associated with a higher prevalence of cataracts (over 2 and 4 times higher, respectively). The team calculated that the people with both low plasma selenium and high blood mercury were 16 times more likely to develop cataracts than the "optimum situation" group, which had both high plasma selenium and low blood mercury.

This is the first study known to associate high levels of methylmercury from fish consumption with increased occurrence of cataracts. The authors emphasize that other factors—such as differences in dietary intakes of antioxidants and vitamins—could confound their findings. Still, if the observed associations hold true in broader studies, public health interventions to alleviate cataracts in this Amazonian population must consider both the health benefits of fish consumption and the risks of the main source of dietary selenium in the region: brazil nuts, which also contain barium and strontium, heavy metals with their own hazards.

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Women and children from a Tapajós village clean fish, a chief component of the local diet, which also includes rice, manioc flour, fruits, and brazil nuts.

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