Mold in Maize

Less Exposure May Mean Less Cancer

Mold-produced toxins have tainted food crops probably since the beginnings of agriculture. These mycotoxins can occur when certain molds infect food crops before or after harvest. Both humans and animals are vulnerable to poisoning through consumption of contaminated foods, with acute or chronic illness—including cancer—a potential result. A study by Paul K. Chelule of the University of Natal in Durban, South Africa, and colleagues focuses on the link between exposure to fumonisin B_1, a mycotoxin produced by *Fusarium verticillioides*, and risk of esophageal cancer [*EHP* 109:253–256].

In the 1980s, researchers from the Medical Research Council of South Africa discovered a highly suggestive link between esophageal cancer and exposure to fumonisin B_1. Because *F. verticillioides* infects maize, a staple crop throughout the world, large populations may be exposed to fumonisin B_1. The work initiated in the 1980s focused on the high incidence of esophageal cancer in certain districts of the Transkei region of South Africa. A key difference between these districts and control areas was that maize in the areas with high cancer rates was highly contaminated with fumonisin B_1. Similar observations were later made elsewhere, notably in China.

The study by Chelule and colleagues looks at fumonisin B_1 exposure among urban and rural populations in KwaZulu Natal province. The researchers wanted to see how fumonisin B_1 exposure among people of KwaZulu Natal compares to that of the Transkei populations, which could indicate whether their potential risk for esophageal cancer is as high. The researchers conclude that the KwaZulu Natal populations encounter lower levels of fumonisin B_1 contamination overall, although rural people have a greater risk of exposure than urban ones.

Eighty-four people took part in the study, 44 from the Durban metropolitan area and 40 from the Tugela Valley, a rural area about 200 kilometers north of Durban. The researchers collected samples of unprocessed maize and sorghum from each person's home, as well as prepared foods including *phutu* (cooked milled maize), *amahewu* (a nonalcoholic fermented gruel-like drink made from maize), and *isizulu* (an alcoholic fermented drink made from maize and sorghum). Fecal samples were also collected from study participants.

Unsavory stew. Exposure to mold-produced toxins in staple crops such as maize raises the risk of esophageal cancer.

The differences observed between unprocessed rural and urban maize samples were significant. Not only were a higher percentage of rural samples contaminated (32% compared to 6%), but the level of contamination was also greater, as determined by chemically extracting fumonisin B_1 from the food and drink samples and analyzing the quantity extracted. This finding translates to the rural population having a 6 times higher risk of fumonisin B_1 exposure—and potential consequences—than the urban population, say the researchers. However, they note that even the highest mycotoxin level found in this study, 22.2 milligrams per kilogram of grain, falls far short of that measured in the Transkei study, which exceeded 117 milligrams per kilogram. None of the sorghum samples from either urban or rural areas contained detectable amounts of fumonisin B_1, and among the cooked foods only rural *phutu* was contaminated. Of the rural fecal samples, 33% had measurable amounts of fumonisin B_1 as compared to 7% of the urban samples. The researchers note that fecal analysis provides a useful short-term indicator for fumonisin B_1 exposure.

The researchers conclude that the people of KwaZulu Natal have a lower risk of fumonisin B_1 exposure and the potentially related esophageal cancer than the people of Transkei. They attribute urban–rural differences in this study to a more varied diet and greater likelihood of food safety regulations in urban areas. Further, given that sorghum is less prone to contamination, they suggest that their results might encourage cultivating sorghum rather than maize in the Tugela Valley. However, they caution that further study is necessary before taking such a step. **–Julia R. Barrett**

Arsenic and Endocrines

New Study Suggests Disruption

Chronic low-level human exposure to arsenic is associated with increased cancer risk. Epidemiologic studies of exposed populations in Asia and South America have shown a significant increase in the risk of skin, lung, liver, and bladder cancers, yet arsenic's carcinogenic mechanism remains unknown. Chronic exposure to arsenic also is associated with elevated risks of type 2 diabetes mellitus and vascular disease. In this issue, Ronald Kaltreider, Joshua Hamilton, and colleagues from Dartmouth Medical School in Hanover, New Hampshire, may have uncovered a clue to a central mechanism behind arsenic's myriad adverse health effects [*EHP* 109:245–251].

Low-level exposure to arsenic in drinking water is widespread in the United States and elsewhere. In New Hampshire, for instance, where 40% of the population's water supply comes from private wells, as much as 8% of the state (one-fifth of all private well users) may be exposed to arsenic concentrations between the U.S. Environmental Protection Agency's proposed standard of 10 parts per billion and the current standard of 50 parts per billion. At industrial sites and toxic waste sites—including over 70% of all Superfund waste sites—arsenic is usually found in combination with many other toxic chemicals, and it can leach into groundwater and find its way into drinking water.

The current study follows up on previous research that found that arsenic affects expression of the well-characterized phosphoenolpyruvate carboxykinase gene in rat liver cancer cells, reducing its responsiveness to hormone signals. Working in Hamilton's laboratory, which studies the effects of toxic metals on gene expression, Kaltreider and colleagues studied three sets of rat liver cancer cells. The first set was treated with various noncytotoxic concentrations of arsenite solution. The second was treated with a synthetic glucocorticoid hormone called dexamethasone (Dex). The third was treated with both arsenite and Dex. Glucocorticoids mediate a large array of effects. Among them are blood glucose regulation, vascular function, cell differentiation, and apoptosis, all of which are key functions in systems affected by arsenic exposure.

The researchers found that low doses of arsenic blocked the glucocorticoid receptor (GR) from responding to its normal hormone signal. More specifically, the researchers found that arsenic selectively disrupted the ability of GR in exposed cells to regulate the expression of its target genes in the nucleus, with the highest arsenite dose causing a greater than 50% suppression in Dex-inducible expression. Arsenite did not appear to interfere with the binding of Dex to GR or with the ability of Dex to activate GR and cause it to migrate to the nucleus. However, once inside the nucleus GR was unable to stimulate gene expression, even though it was fully activated by Dex.

Arsenic thus appears to act as a new class of endocrine disruptor by altering certain aspects of receptor function, even in nontoxic doses. GR is a critical player in mediating blood glucose regulation, so disrupting that function could be a part of how arsenic affects diabetes. GR is also an important regulator of normal vascular function, so disrupting GR in these tissues may contribute to how arsenic causes vascular disease. Finally, GR has been shown in animal and cell culture studies to play a crucial role in the cancer process in both the skin and the lung—both of which are targets for arsenic-induced carcinogenesis—and loss of GR function in animal tumor models has been shown to promote the cancer process in both tissues. The researchers therefore theorize that arsenic's action as an endocrine disruptor, although perhaps not the only mechanism, may be an important contributing factor in several different arsenic-related diseases.

Arsenic's effects also seem to be highly specific for GR-induced gene expression. Kaltreider and colleagues are currently investigating whether binding of arsenic to GR directly causes the alterations in GR function. They suggest that possible effects of arsenic on other steroid receptors such as those for estrogen and progesterone should be investigated to determine whether arsenic's effects are specific to GR or a general effect on this family of hormone receptors. **–Julian Josephson**

From Animal Feed to People Food

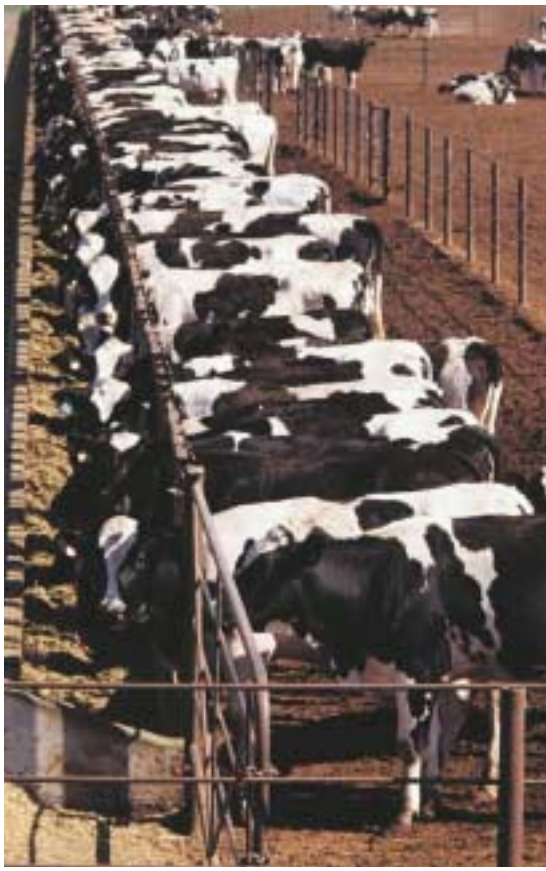
The Belgian Dioxin Incident

In January 1999, animal feedlots in Belgium were contaminated with polychlorinated biphenyls (PCBs) and dioxins including polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans. The dioxins, probably originating from oil left at a waste recycling center, entered the food supply via animal feed made with recycled animal fat. (In Belgium, waste fat from recycling centers is commonly mixed with fat from slaughterhouses to make animal feed.) Five hundred tons of the contaminated feed was distributed to farms, mostly poultry operations, throughout Belgium. In this issue, Nik van Larebeke and colleagues from four Flemish universities conclude that the incident may have doubled or tripled the PCB/dioxin body burden of some Belgians [*EHP* 109:265–273].

News of the incident broke in late May, sparking a public outcry and a scramble by government agencies to assess the human health damage. The Ministries of Public Health and Agriculture ordered testing of over 20,000 samples of beef, pork, poultry, eggs, milk, and fat-containing processed foods found on Belgian grocery shelves. The sampling, conducted between May and August 1999, analyzed the health impact of the contaminants on consumers and provided the materials for the current study.

Dioxins, a group of chemical compounds released by processes such as waste incineration and the burning of household fuel, have been linked to health effects ranging from skin disease to cancer. PCBs are mixtures of synthetic organic chemicals. Like dioxins, PCBs have been linked to cancer; they have also been associated with neurotoxicity, reproductive and developmental toxicity, immune suppression, liver damage, skin irritation, and endocrine disruption.

Van Larebeke and colleagues sorted the food samples into three categories: those traceable to farms that used contaminated feed, those traceable to farms that did not use contaminated feed, and those for which a link with the contamination incident could not be clearly established. The sampling effort by 23 labs measured dioxins with mass spectrometry and quantified PCBs using gas chromatographic techniques along with electron capture or mass spectrometry.



How now, cow chow? PCBs and dioxins taken up by livestock that ate contaminated feed may have doubled or tripled the PCB/dioxin body burden of some Belgians.

Compared with dioxin incidents elsewhere, the Belgian incident exposed more people but to much smaller amounts of dioxins. The analysis suggests that in terms of added cancer risk, the incident could result in 32–1,540 additional cancer deaths over the projected lifetime of the total Belgian population of 10 million, and PCB exposure could add between 22 and 6,545 cancer deaths. These ranges are based on applying two different risk estimates for lifetime exposure to the amount of contaminants in the incident exposure.

Depending on a person's diet and the chance occurrence of high levels of contamination, however, the effects could be much more serious. The potential impacts of three common dietary patterns typical of the average Belgian citizen were assessed. One pattern assumed the ingestion of 15 grams of heavily contaminated animal fat per day and resulted in a 75% increase in dioxin body burden. Another assumed the ingestion of three portions of heavily contaminated chicken meat per week and resulted in a 42% increase in dioxin body burden. A third common dietary pattern resulted in a 48% increase in dioxin body burden. Some people may have incurred even higher exposures because consumption of products such as milk and derived food items such as sauces and pastries were not factored in to the estimations.

The 1999 Belgian dioxin incident added further risk to background levels that were already high. The authors warn that significant numbers of Belgians who consumed contaminated products temporarily increased their intake of dioxins to a level up to 100 times greater than that recommended by the World Health Organization. Furthermore, conclude the authors, the long-term effects may be particularly hard to detect because of the high background levels. The researchers recommend further monitoring of exposed populations and stricter chemical and physical hygiene, including better screening of materials left at recycling centers. **–David A. Taylor**

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