

Extramural papers of the month

By Nancy Lamontagne

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Read the current
Superfund Research Program
Research Brief. New issues
are published on the first
Wednesday of each month.

Olestra reduces PCBs in the body

According to a study funded in part by NIEHS, the zero-calorie fat substitute olestra can speed the removal of polychlorinated biphenyls (PCBs) from the body. The findings suggest that olestra could offer a low-risk dietary intervention for people exposed to PCBs.

Olestra is a nonabsorbable fat substitute introduced in snack foods in 1996. Animal studies have suggested that olestra could increase the rate that organochlorines, such as PCBs, are cleared from the body. The researchers tested its effectiveness in 28 people with high levels of PCBs. All of them lived in Anniston, Alabama, site of a plant that manufactured PCBs for 40 years.

During the yearlong study, half of the participants consumed, per day, 12 Pringles brand potato chips made with vegetable oil, and the other half consumed, per day, 24 Pringles made with olestra. Total daily intake of olestra was 15 grams. The serving sizes were different, to help equalize calorie consumption between the test groups. Overall, the rate of PCB clearance from the participants who ate the chips made with olestra was faster during the one-year trial than before the trial. Two participants in the olestra group showed a decrease in concentration of PCBs of 27 percent and 25 percent during the trial. The researchers suggest that olestra apparently makes fat-soluble compounds, like PCBs in the intestine, more likely to be dissolved, reducing absorption of these compounds into the body.

Citation: Jandacek RJ, Heubi JE, Buckley DD, Khoury JC, Turner WE, Sjodin A, Olson JR, Shelton C, Helms K, Bailey TD, Carter S, Tso P, Pavuk M.

(<http://www.ncbi.nlm.nih.gov/pubmed/24629911>)

2014. Reduction of the body burden of PCBs and DDE by dietary intervention in a randomized trial. *J Nutr Biochem* 25(4):483-488.

Activation and regulation of polymerase V during DNA synthesis

When a cell's DNA replication machinery reaches damaged DNA, it must either repair or bypass the damage to copy its genome. In *E. coli*, the enzyme polymerase V can copy past damaged DNA, but it often introduces new mistakes when copying undamaged DNA. NIEHS grantees have discovered new details about the molecular basis for polymerase V activation, and a unique regulatory mechanism that limits polymerase V synthesis to the short DNA segments where it is needed. Understanding the role of DNA polymerases, in either inducing or preventing mutations, will have wide-ranging implications for understanding disease initiation or progression, and individual susceptibility, as well as determining treatment and prevention strategies.

The investigators used biochemical techniques to better understand how binding to the RecA protein and adenosine triphosphate (ATP) activates polymerase V. They found that the enzyme must bind to an ATP molecule before attaching to the DNA, and it must remain bound to ATP during DNA synthesis. The enzyme then breaks down the molecule of ATP to free itself from the DNA. Although the RecA protein can also break down ATP, the researchers found that mutant RecA lacking this ability can still trigger DNA polymerase V to break down ATP itself.

No DNA polymerase has been observed to be regulated by ATP in this way. According to the researchers, this extra control would limit DNA polymerase V to only copying damaged DNA, and keep it from copying neighboring stretches of undamaged DNA where it would likely introduce new errors.

Citation: Erdem AL, Jaszczur M, Bertram JG, Woodgate R, Cox MM, Goodman MF.

(<http://www.ncbi.nlm.nih.gov/pubmed/24843026>)

2014. DNA polymerase V activity is autoregulated by a novel intrinsic DNA-dependent ATPase. *eLife* 3:e02384.

SSRI use during pregnancy associated with autism

New results from the NIEHS-funded Childhood Autism Risks from Genetics and the Environment (CHARGE) study show an association between prenatal exposure to selective serotonin reuptake inhibitors (SSRIs) and autism spectrum disorder, as well as developmental delays in boys. SSRIs are a frequently prescribed treatment for depression, anxiety, and other disorders.

The researchers examined 966 mother-child pairs participating in the CHARGE study and found that prenatal SSRI exposure was nearly three times as likely in boys with autism spectrum disorder, compared to boys with typical development, with the greatest risk occurring if exposure took place during the first trimester. SSRI use was also elevated among boys with developmental delays, with the strongest exposure effect in the third trimester.

The researchers acknowledge limitations of the study, including the difficulty of isolating SSRI effects from those of their indications for use, as well as the relatively small sample of children with developmental delays. They also note that because maternal depression also carries risks for the fetus, the benefits of prenatal SSRI use should be carefully weighed against potential risks.

Citation: [Harrington RA, Lee LC, Crum RM, Zimmerman AW, Hertz-Picciotto I.](#)

(<http://www.ncbi.nlm.nih.gov/pubmed/24733881>)

2014. Prenatal SSRI use and offspring with autism spectrum disorder or developmental delay. *Pediatrics* 133(5):e1241-e1248.

Coal-burning stoves in Mongolia linked to seasonal variance in miscarriages

According to research funded by NIEHS, pollution from the coal-burning stoves used in Ulaanbaatar, Mongolia, for winter heating, is strongly associated with miscarriages. Ulaanbaatar is the coldest capital city in the world, and one of the most air polluted.

To examine the association between miscarriages and seasonal variation of air pollutants, the investigators used measurements from Mongolian Government Air Quality Monitoring stations, and medical records of 1,219 women admitted to the hospital due to miscarriage. The overall rate of miscarriage reported in Ulaanbaatar was similar to that of Western countries, but miscarriages, per calendar month, increased from 23 per 1,000 live births in May 2011 to 73 per 1,000 live births in December 2011. Monthly average ambient levels of air pollutants increased in relation to hours of darkness and coldest temperatures, when the coal heating stoves are used most. Regression analysis of ambient pollutants against fetal death revealed dose-response correlations for sulfide dioxide $r^2 > 0.9$ ($p < 0.001$), nitrogen dioxide ($r^2 > 0.8$), carbon monoxide ($r^2 > 0.9$), PM 10 ($r^2 > 0.9$) and PM 2.5 ($r^2 > 0.8$), ($p < 0.001$), indicating a strong correlation between air pollution and decreased fetal wellbeing.

Although major policy changes are helping to curb air pollution in Mongolia, the researchers speculate that up to five-fold further reduction in air pollutants in winter would be needed, to reduce fetal death rates to levels experienced during the summer in Ulaanbaatar.

Citation: [Enkhmaa D, Warburton N, Javzandulam B, Uyanga J, Khishigsuren Y, Lodoysamba S, Enkhtur S, Warburton D.](#)

(<http://www.ncbi.nlm.nih.gov/pubmed/24758249>)

2014. Seasonal ambient air pollution correlates strongly with spontaneous abortion in Mongolia. *BMC Pregnancy Childbirth* 14(1):146.

(Nancy Lamontagne is a science writer with MDB Inc., a contractor for the NIEHS Division of Extramural Research and Training.)

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(bruscek@niehs.nih.gov)

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