

NIEHS researchers show low doses of arsenic cause cancer in male mice

By Robin Mackar

Michael Waalkes, Ph.D., knows how to end his career on a high note. Waalkes was head of National Toxicology Program (NTP) Laboratory until his retirement in June, after 31 years of federal service. He and his colleagues in NTP published a [paper](#)

(<http://www.ncbi.nlm.nih.gov/pubmed/25005685>)

July 9 in the journal Archives of Toxicology with far-reaching impact, showing that mice exposed to low doses of inorganic arsenic in drinking water, similar to what some people might consume, developed lung cancer.

Whole life model duplicates human exposure

The Waalkes team used a model that mimics how humans are exposed to arsenic over their lifetime. Mice were given arsenic in their drinking water three weeks before breeding, as well as throughout pregnancy and lactation. Arsenic was then given to the offspring after weaning, and all through adulthood, at concentrations relevant to human exposure. The researchers then examined tumors in the adult offspring.

Concentrations in the drinking water were 50 parts per billion (ppb), 500 ppb, and 5,000 ppb. The 50 ppb dose is the lowest concentration tested in an animal study, and many researchers feel that differing rates of metabolism and excretion mean that mice need to be exposed to greater concentrations than humans to achieve similar internal doses.

"This is the first study to show tumor development in animals exposed to very low levels of arsenic - levels similar to which humans might be exposed," said Waalkes. "The results are unexpected and certainly give cause for concern."

Arsenic is present in the environment, both as a naturally occurring substance and due to contamination from human activity. Arsenic may be found in many foods, including grains, fruits, and vegetables, due to plant absorption from soil and water. This study focused on inorganic arsenic, which occurs in the drinking water of millions of people worldwide and is known to be a human carcinogen that targets the lung and several other sites. More information about arsenic can be found in a newly developed NIEHS [fact sheet](#).

Findings add to growing evidence of low dose effects

More than half of the male offspring in the study developed significant increases in benign and malignant lung tumors at the two lower doses (50 ppb and 500 ppb). Female offspring also developed benign tumors at the lower concentrations. Interestingly, the researchers did not find significant increases in lung tumors in either sex at the highest dose (5,000 ppb).

"Although this is only one study, it adds to a growing body of evidence showing adverse health effects from very low exposures to arsenic, raising the possibility that no level of arsenic appears to be safe," said Linda Birnbaum, Ph.D., director of the NIEHS and NTP.

Citation: Waalkes MP, Qu W, Tokar EJ, Kissling GE, Dixon D.

(<http://www.ncbi.nlm.nih.gov/pubmed/25005685>)

2014, Lung tumors in mice induced by "whole-life" inorganic arsenic exposure at human-relevant doses. Arch Toxicol 88(8):1619-1629.

(Robin Mackar is the news director in the NIEHS Office of Communications and Public Liaison and a regular contributor to the Environmental Factor.)



The study is a paradigm shift for low dose studies, said Waalkes, who is known for his research capabilities and mentoring of future scientists. (Photo courtesy of Steve McCaw)



Erick Tokar, Ph.D., biologist in the NTP Inorganic Toxicology Group and a co-author on the paper, presented the new findings to Her Royal Highness Princess Chulabhorn of Thailand, founder and president of the Chulabhorn Research Institute, during her visit July 11 to NIEHS (see [story](#)). (Photo courtesy of Steve McCaw)

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