

From: Steve Lamm
Sent: Tuesday, January 24, 2006 3:53 PM
To: 'Miller.Tom@epa.gov'
Subject:

Tom,

This is my pubmed search on Uthus and arsenic.

Steve Lamm

1: [J Inorg Biochem.](#) 2005 Jun;99(6):1269-74.

Related Article

Mechanistic aspects of the interaction between selenium and arsenic.

[Zeng H](#), [Uthus EO](#), [Combs GF Jr](#).

Agricultural Research Service, Grand Forks Human Nutrition Research Center, United States Department of Agriculture, 2420, 2nd Avenue, Grand Forks, ND 58202-9034, USA. hzenng@gfhnrc.ars.usda.gov <hzenng@gfhnrc.ars.usda.gov>

Selenium is an essential trace element for humans and other animals, and there is mounting evidence for the efficacy of certain forms of selenium as cancer-chemopreventive compounds. However, over the years, numerous elements such as As, Cu, Zn, Cd, Hg, Sn, Pb, Ni, Co, Sb, Bi, Ag, Au, and Mo have been found to inhibit anti-carcinogenic effects of selenium, which may affect the anti-carcinogenic activity of selenium. The interaction between selenium and arsenic has been one of the most extensively studied. The proposed mechanisms of this interaction include the increase of biliary excretion and direct interaction/precipitation of selenium and arsenic, and their effects on zinc finger protein function, cellular signaling and methylation pathways. This article focuses on these proposed mechanisms and how anti-carcinogenic effects of selenium may be affected by arsenic.

Publication Types:

- [Review](#)

PMID: 15917080 [PubMed - indexed for MEDLINE]

2: [Biol Trace Elem Res.](#) 2005 Feb;103(2):133-45.

Related Article

Dietary arsenic affects dimethylhydrazine-induced aberrant crypt formation and hepatic global DNA methylation and DNA methyltransferase activity in rats.

[Uthus EO](#), [Davis C](#).

United States Department of Agriculture, ARS, Grand Forks Human Nutrition Research Center, Grand Forks, ND 58202, USA.

Cell culture studies have suggested that arsenic exposure results in decreased S-adenosylmethionine (SAM), causing DNA hypomethylation. Previously, we have shown that hepatic SAM is decreased and/or S-adenosylhomocysteine increased in arsenic-deprived rats; these rats tended to have hypomethylated DNA. To determine the effect of dietary arsenic on dimethylhydrazine (DMH)-induced aberrant crypt formation in the colon, Fisher 344 weanling male rats were fed diets containing 0, 0.5, or 50 microg As (as NaAsO₂)/g. After 12 wk, dietary arsenic affected the number of aberrant crypts ($p < 0.02$) and aberrant crypt foci ($p < 0.007$) in the colon and the amount of global DNA methylation ($p < 0.04$) and activity of DNA methyltransferase (DNMT) ($p < 0.003$) in the liver. In each case, there were more aberrant crypts and aberrant crypt foci, a relative DNA hypomethylation, and increased activity of DNMT in the rats fed 50 microg As/g compared to those fed 0.5 microg As/g. The same phenomenon, an increased number of aberrant crypts and aberrant crypt foci, DNA hypomethylation, and increased DNMT tended to hold when comparing rats fed the diet containing no supplemental arsenic compared to rats fed 0.5 microg As/g. The data suggest that there is a threshold for As toxicity and that possibly too little dietary As could also be detrimental.

PMID: 15772437 [PubMed - indexed for MEDLINE]

3: [J Nutr](#). 2000 Dec;130(12):2903-9.

[Related Article](#)

Comment in:

- [J Nutr](#). 2001 Jun;131(6):1871-2.

Dietary selenium and arsenic affect DNA methylation in vitro in Caco-2 cells and in vivo in rat liver and colon.

[Davis CD](#), [Uthus EO](#), [Finley JW](#).

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Selenium is an essential trace element for human health, and it has received considerable attention for its possible role as an anticarcinogenic agent. The purpose of the present study was to determine whether changes in the amount and the chemical form of selenium would affect DNA methylation and whether this effect would be modified by arsenic. Caco-2 cells, a human colon cancer cell line, were exposed to 0, 1 or 2 micromol supplemental selenite/L and 0, 1 or 2 micromol supplemental arsenite/L for 7 d. DNA isolated from Caco-2 cells not treated with selenite was significantly ($P < 0.0001$) hypomethylated compared with that from cells treated with 1 or 2 micromol selenite/L. DNA isolated from Caco-2 cells not treated with arsenite was significantly ($P < 0.0001$) hypomethylated compared with DNA isolated from cells treated with 1 or 2 micromol arsenite/L. In addition, methylation of the p53 promoter region of Caco-2 cells decreased when cells were cultured in the absence of selenite and in the absence of arsenite. Sixty weanling male Fischer 344 rats were fed a torula yeast-based diet supplemented with 0, 0.1 or 2 mg selenium/kg diet as either selenite or selenomethionine in the presence or absence of 5 mg arsenic/kg diet as arsenite for 6 wk. Similar to the results with Caco-2 cells, rats fed selenium-deficient diets had significantly ($P < 0.0001$) hypomethylated liver and colon DNA compared with rats fed 0.1 or 2.0 microg selenium/g diets as either selenite or selenomethionine. Thus, alterations in DNA methylation may be a potential mechanism, whereby deficient dietary selenium increases liver and colon tumorigenesis.

PMID: 11110844 [PubMed - indexed for MEDLINE]

4: [J Nutr.](#) 1996 Sep;126(9 Suppl):2452S-2459S.

Rela

Deliberations and evaluations of the approaches, endpoints and paradigms for dietary recommendations of the other trace elements.

[Uthus EO](#), [Seaborn CD](#).

United States Department of Agriculture, Agricultural Research Service, Grand Forks Human Nutrition Research Center, ND 58202, USA.

Circumstantial evidence suggests that aluminum, arsenic, bromine, cadmium, germanium, lead, lithium, nickel, rubidium, silicon, tin and vanadium are essential. The evidence is most compelling for arsenic, nickel, silicon and vanadium. The estimated daily dietary intakes for these elements are arsenic, 12-50 micrograms; nickel, 100 micrograms; silicon, 20-50 mg and vanadium, 10-20 micrograms. By extrapolation from animal studies, the daily dietary intakes of these elements needed to prevent deficiency or to provide beneficial action in humans are arsenic, 12-25 micrograms; nickel, 100 micrograms; silicon, 2-5 mg (based on 10% bioavailability in natural diets) and vanadium, 10 micrograms.

Thus, the postulated need by humans for these elements can be met by typical diets. Because there may be situations, however, where dietary intake does not meet the postulated requirements, research is needed to derive status indicators in humans and to further study the relationships of low intake or impaired bioavailability of these ultratrace elements to various diseases.

PMID: 8811811 [PubMed - indexed for MEDLINE]

5: [Biol Trace Elem Res](#). 1994 Dec;46(3):247-59.

Rela

Diethyl maleate, an in vivo chemical depletor of glutathione, affects the response of male and female rats to arsenic deprivation.

[Uthus EO](#).

United States Department of Agriculture, Grand Forks Human Nutrition Research Center, ND 58202-9034.

An experiment was performed to determine the effect of diethyl maleate (DEM), an in vivo depletor of glutathione, on the response of male and female rats to arsenic deprivation. A 2 x 2 x 2 factorially arranged experiment used groups of six weanling Sprague-Dawley rats. Dietary variables were arsenic at 0 or 0.5 microgram/g and DEM at 0 or 0.25%; the third variable was gender. Animals were fed for 10 wk a casein-ground corn based diet that contained amounts of calcium, phosphorus, and magnesium similar to the AIN-76 diet. DEM supplementation increased blood arsenic in both male and female rats; female rats had the greatest amount of arsenic in whole blood. Although female rats in general had a lower concentration of glutathione in liver, those fed no supplemental DEM, regardless of their arsenic status, had the lowest amounts. Compared to males, female rats had a lower activity of liver glutathione S-transferase (GST). Arsenic deprivation decreased, and DEM supplementation increased liver GST activity in both male and female rats. Lung GST activity was also increased by DEM supplementation in male, but not female, rats. The most striking finding of the study was that compared to males, females had extremely elevated kidney calcium concentrations, and that the elevation was exacerbated by arsenic deprivation. DEM supplementation also exacerbated the accumulation of calcium in the kidney of the female rats. The response of the rat to both DEM and arsenic was, for many variables, dependent on gender. This gender dependence may be explained by the differences in methionine metabolism between male and female rats. Thus, arsenic deprivation apparently can manifest itself differently depending on gender.

PMID: 7702979 [PubMed - indexed for MEDLINE]

6: [Scand J Work Environ Health](#). 1993;19 Suppl 1:137-8.

Determination of the possible requirement and reference dose levels for arsenic in humans.

[Uthus EO](#), [Nielsen FH](#).

USDA, Grand Forks Human Nutrition Research Center, ND 58202.

PMID: 8159966 [PubMed - indexed for MEDLINE]

7: [Magnes Trace Elem](#). 1991-92;10(5-6):339-47.

Effect of dietary pyridoxine on arsenic deprivation in rats.

[Uthus E](#), [Poellot R](#).

USDA, Grand Forks Human Nutrition Research Center, N. Dak.

A study was performed to determine whether dietary pyridoxine affects the response of rats to arsenic deprivation. A 2 x 2 x 2 factorially arranged experiment utilized groups of 6 male weanling Sprague-Dawley rats. They were fed a 14% amino acid/76% acid-washed corn diet for 10 weeks. The dietary variables were arsenic, 0 or 1 microgram/g; pyridoxine.HCl, 0 or 10 mg/kg, and L-methionine, 0 or 3 g/kg. The basal diet contained 0.24% methionine (calculated) and about 10 ng arsenic/g. Growth was reduced by arsenic, pyridoxine or methionine deprivation. Other parameters including blood indices, erythrocyte aspartate aminotransferase and the concentration of tissue iron and plasma amino acids were affected by dietary arsenic, pyridoxine, methionine or their interaction. The data demonstrate that dietary pyridoxine and arsenic interact and that the methionine status of the animal can affect this interaction.

PMID: 1669017 [PubMed - indexed for MEDLINE]

8: [Magnes Trace Elem](#). 1990;9(4):227-32.

Effects of arsenic deprivation in hamsters.

[Uthus EO](#).

United States Department of Agriculture, Grand Forks Human Nutrition Research Center, Grand Forks.

An experiment was conducted to ascertain the effects of arsenic deprivation in hamsters. Male weanling Golden Syrian hamsters were fed a casein-corn-based diet containing approximately 12 ng arsenic/g. Controls were fed 1 microgram arsenic/g of diet, as Na₂HAsO₄·7 H₂O. After 6 weeks arsenic deprivation elevated heart weight/body weight ratio and the concentration of liver zinc and decreased the concentrations of the plasma amino acids alanine, glycine, phenylalanine and taurine. Although no biological role has been found for arsenic, the findings indicate that the hamster is a suitable animal for arsenic deprivation studies and support the hypothesis that arsenic may have a physiological role that influences methionine/methyl metabolism.

PMID: 2095167 [PubMed - indexed for MEDLINE]

9: [Anal Chem.](#) 1981 Dec;53(14):2221-4.

Related Ar

Determination of total arsenic in biological samples by arsine generation and atomic absorption spectrometry.

[Uthus EO](#), [Collings ME](#), [Cornatzer WE](#), [Nielsen FH](#).

PMID: 7316211 [PubMed - indexed for MEDLINE]

10: [Ann N Y Acad Sci.](#) 1980;355:152-64.

Related A

Interactions between essential trace and ultratrace elements.

[Nielsen FH](#), [Hunt CD](#), [Uthus EO](#).

Fully crossed, factorially arranged experiments showed that, under defined conditions, interactions occur between nickel and iron, nickel and copper, arsenic and zinc, and possibly vanadium and chromium. Nickel and iron interacted when dietary iron was supplemented as ferric sulfate only. Signs of nickel deprivation were more severe when dietary iron was low; or the signs of moderate iron deficiency were more severe when dietary nickel was deficient. When iron was supplemented to the diet as a 60% ferric-40% ferrous sulfate mixture, nickel and iron apparently did not interact. The findings suggested a synergistic relationship between nickel and iron when dietary iron was in a relatively unavailable form. An antagonistic interaction between nickel and copper was found when dietary iron was supplemented as a 60% ferric-40% ferrous sulfate mixture. Signs of copper deficiency were more severe in nickel-supplemented than in nickel-deprived rats. When the rats were made severely iron deficient by feeding of low levels of ferric sulfate only, no apparent interaction between nickel and copper was found. The interaction between arsenic and zinc apparently was

noncompetitive. When dietary zinc was 40 microgram/g, arsenic-deprived chicks exhibited depressed growth and elevated hematocrits. In zinc deficiency, growth was more markedly depressed and hematocrits more markedly elevated in arsenic-supplemented than in arsenic-deficient chicks. Arsenic might be necessary for the efficient utilization or metabolism of zinc. Findings indicating an interaction between vanadium and chromium were tentative. In one experiment, the addition of 500 microgram of chromium/g of diet apparently made 5 micrograms of vanadium/g of diet toxic for chicks. Thus, the interactions between essential trace and ultratrace elements might be of nutritional significance.

PMID: 6940472 [PubMed - indexed for MEDLINE]