Arsenic biomethylation required for oxidative DNA damage

November 23 2009

Biomethylation of arsenic compounds appears to cause oxidative DNA damage and to increase their carcinogenicity, according to a new study published online November 23 in the *Journal of the National Cancer Institute*.

Although biomethylation was once believed to detoxify inorganic arsenic , it is now thought to enhance its toxicity and potentially its carcinogenicity.

To assess the role of arsenic biomethylation in oxidative DNA damage in mice, Michael P. Waalkes, Ph.D., of the National Cancer Institute at the National Institute of Environmental Health Sciences, and colleagues compared oxidative DNA damage in methylation-competent cell lines vs. methylation-deficient cell lines exposed to arsenic.

Exposure of the methylation-competent cells, but not methylation-deficient cells, was followed by a sharp rise in oxidative DNA damage. Subsequent to the peak of oxidative DNA damage, methylation-competent cells, more rapidly than methylation-deficient cells, acquired the in vitro characteristics of cancer cells.

Animals have been engineered not to biomethylate arsenic. "Although inorganic arsenicals have not yet been tested for carcinogenic effects in these genetically altered mice, this clearly should be a high priority," the authors write.

In an accompanying editorial, Michael F. Hughes, Ph.D., of the Environmental Protection Agency, in Research Triangle Park, N.C., reviews the history of research concerning arsenic methylation and its role in carcinogenesis. He notes that future investigations will need to determine whether arsenic-induced oxidative stress contributes to arsenic-induced toxicity and carcinogenesis by affecting cell signaling pathways and/or apoptosis.

Source: Journal of the National Cancer Institute (news : web)