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Dermal Absorption of Inorganic Arsenic from Water

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Abstract

The question of the potential for exposure to inorganic arsenic in water through dermal contact is important when providing guidance about treatment options to private well owners. If dermal contact with the water is an exposure route of concern, then whole house treatment is required, while if only oral exposure is considered, then treatment at the kitchen tap will be sufficient. For this reason, a review of the available information on absorption of inorganic arsenic from water via the dermal route was undertaken.

Two recent reviews, the National Research Council's report, Arsenic in Drinking Water (NRC, 1999), and the Agency for Toxic Substances and Disease Registry's, Toxicological Profile for Arsenic (ATSDR, 2000), evaluated the limited available information on dermal exposure to inorganic arsenic. In addition to the studies cited in these reviews, literature searches were performed to locate any additional and/or more recent information on this subject.

Neither the National Research Council (1999) or the Agency for Toxic Substances and Disease Registry (2000), nor the additional literature searches, identified any controlled studies of inorganic arsenic absorption through human skin. A few studies have evaluated the absorption of arsenic through the skin of laboratory animals and humans in vitro and laboratory animals in vivo, and limited information is available on arsenic exposures in individuals using wells with elevated arsenic levels for bathing, but not drinking.

Dutkiewicz (1977) studied the absorption of arsenic in vivo by immersing the tails of female Wistar rats in solutions of 0.01, 0.1, or 0.2 M radiolabelled sodium arsenate for one hour. The animals were sacrificed at time points from one hour to 10 days after exposure. Arsenic was not detected in the blood or tissues for up to 24 hours after exposure, but increased in blood, liver, and spleen over the next 5 days. It was concluded that the arsenic bound to the skin during the exposure period, and was slowly taken up after the exposure ceased. The author calculated that the absorption of arsenic through skin at 0.01 M - 0.2 M concentrations was 1.14 ug/cm^2 skin x hr - 33.1 ug/cm^2 skin x hr.

Wester et al. (1993) studied the skin absorption of inorganic arsenic, using radiolabelled arsenic acid, in vivo in Rhesus monkeys and in vitro in skin from human cadavers. In the monkey studies, a small volume (5 ul/cm^2 skin) of the arsenic-containing solution was applied to the abdominal skin. Two arsenic concentrations were used, which differed by 5 orders of magnitude (0.000024 ug/cm^2 and 2.1 ug/cm^2). The application site was covered for 24 hours, after which the cover was removed and the skin was washed with soap and water. Urine was collected for 7 days, and the percentage of the dose absorbed was calculated by comparison to percent excreted over 7 days in an intravenous dose (to account for non-urinary excretion and retention in the body). The extent of percutaneous absorption of arsenic was found to be 6.4% for the trace dose and 2.0% for the high dose.

In the study using human skin, Wester et al. (1993) applied the trace dose used above to human cadaver skin samples in flow-through diffusion cells. After 24 hours, arsenic was determined in the receptor fluid and in the skin following washing with soap and water. It was found that 0.93% of the dose had entered the receptor fluid and 0.98% of the dose remained in the skin after washing, indicating a total absorption into the skin of 1.9%.

Rahman et al. (1994) studied the in vitro absorption of radiolabelled sodium arsenate in skin from $B6C3F_1$ mice using flow-through diffusion cells. Sodium arsenate (total mass 5, 50, or 500 ng) was applied to a skin sample of area 0.64 cm^2 in a volume of 100 ul or 250 ul. After 24 hours in the diffusion chamber, the skin was washed repeatedly with water and the arsenic in the skin and in the receptor fluid was determined. It was found that about 62% of the dose was taken up from the 100 ul volume and about 32% from the 250 ul volume, regardless of the dose. When the arsenic was applied in a 100 ul volume, about 60% of the dose which was taken up remained in the skin and the remainder entered the receptor fluid, while when the arsenic was applied in 250 ul volume, about 90% of the dose taken up remained in the skin. The authors also studied the absorption of "solid" arsenate applied in 50 ul of ethanol/water which was quickly evaporated; this condition provided intermediate results between the two water volumes tested. The reason for the great variation in absorption results between the two water volumes tested remain unclear. However, it is interesting that in all cases tested, the percentages absorbed appeared to be independent of the doses of arsenic administered and dependent upon the way the dose was applied (100 ul, 250 ul, or "solid").

As can be seen from the above discussion, the in vitro results of Wester et al. (1993) and Rahman et al. (1994) differ greatly in the percentage of arsenic absorbed. These differences may be due to species differences in skin absorption, as mouse skin has been found to be more permeable in vitro than human cadaver skin to many chemicals (Rahman et al., 1994) and/or to differences in hydration of the skin, as the arsenic was applied in a greatly

differing volume in the two studies.

Smith (2002) estimated the potential dermal absorption by a child bathing in water containing arsenic, using permeability constants for arsenic derived from the rodent studies of Rahman et al. (1994) and Dutkiewicz (1977). In addition, these calculations were independently confirmed by the present author. Since the studies of Rahman et al. (1994) and Dutkiewicz (1977) showed absorption approximately 10-fold higher than the Rhesus monkey and human cadaver skin studies of Wester et al. (1993), they are likely to provide overestimates, rather than underestimates, of human absorption. It was estimated that, from a half hour bath, a child would absorb less than 0.1 ug arsenic at 10 ug/L, less than 1 ug at 100 ug/L, and less than 10 ug at 1000 ug/L. In contrast, 80-90% of an oral dose of inorganic arsenic is absorbed in humans or experimental animals (NRC, 1999). Assuming a child ingests one liter of water per day, the half-hour bath is estimated to contribute less than 1% to the exposure from ingestion.

Further information on the potential for dermal exposure to arsenic through water comes from a study of an Alaskan population with high arsenic levels in their wells (Harrington et al., 1978). The study involved 59 homes and 232 subjects, with arsenic levels in their wells ranging from 1 ug/L to 2450 ug/L. Subjects were classified as bottled water drinkers (average well As level – 345 ug/L + 688 ug/L), "switchers" who had begun to drink bottled water in the three months prior to the study (average As level 498 ug/L + 385 ug/L), well water drinkers with arsenic less than 100 ug/L (average As level 31 ug/L + 33 ug/L), and well water drinkers with arsenic above 100 ug/L (average As level 401 ug/L + 318 ug/L). Levels of arsenic in urine, hair, and nails were measured. It was found that the urinary arsenic levels of the bottled water drinkers and the recent switchers did not differ from the levels in the group with well arsenic levels below 100 ug/L, despite an average well arsenic level more than 10-fold higher than the low well arsenic group. However, the hair arsenic levels of the bottled water drinkers and switchers were similar to those with high well arsenic levels who did not drink bottled water, and about 10-fold higher than those with low arsenic well levels. These results suggest that there is a low degree of skin absorption of arsenic, but that arsenic may bind externally to hair during bathing.

The Wisconsin Department of Natural Resources recently completed a study of health effects of arsenic in drinking water (Knobeloch, 2002). A minor aspect of this study involved measuring urinary arsenic in 15 people (11 adults and 4 children) who did not drink their well water, but continued to bathe in it. The arsenic levels in the wells ranged from 34 ug/L to 3100 ug/L. The subjects did not eat fish or seafood for at least three days before the urine was collected to avoid exposure to "fish arsenic". Arsenic levels from all subjects was within the normal range reported by the laboratory (0-30 ug/L), with 7 nondetectable samples (below 10 ug/L) and the remainder between 10 ug/L and 17 ug/L.

Finally, the Maine Bureau of Health and the U.S. Centers for Disease Control are currently undertaking a study to measure arsenic exposure in adults and children who bathe in, but do not drink, water with elevated levels or arsenic (Smith, 2002). The results of this study will provide further insight into the extent of exposure to arsenic through dermal exposure.

In summary, the literature on dermal absorption of inorganic arsenic from water is quite limited. The laboratory studies suggest that dermal absorption does occur to some extent. In vivo results from the species tested which is most relevant to humans, Rhesus monkeys, as well as the in vitro studies from human cadaver skin, give similar absorption rates, and suggest that the rate of absorption is low. In contrast, in vivo results from the rat and in vitro data from the mouse gave rates of absorption about 10-fold higher. Estimates of potential dermal absorption through bathing indicate that exposure is less than 1% of that received through drinking water, even when the higher rodent dermal absorption data, which is less likely to be relevant to humans are used. If the data from Rhesus monkeys and human cadaver skins are used, the estimates of dermal absorption will be about ten times lower. The limited data from individuals using high arsenic water for bathing and other household uses while drinking bottled water do not demonstrate detectable absorption of arsenic from bathing. The National Research Council (1999) evaluated the available information on this subject and stated that "these results indicate a low degree of systemic absorption of arsenic via the skin." ATSDR (2000) concluded that "it is usually considered that dermal uptake of arsenates and arsenites is sufficiently low that this route is unlikely to be of health concern …, but studies to test the validity of this assumption would be valuable."

References

Agency for Toxic Substances and Disease Registry (2000). Toxicological Profile for Arsenic (Update). PB/2000/108021.

Dutkiewicz, T. (1977). Experimental studies on arsenic absorption routes in rats. Env. Health Perspect. 19: 173-177.

Harrington, J.M., Middaugh, J.P., Morse, D.L, and Housworth, J. (1978). A survey of a population exposed to high concentrations of arsenic in well water in Fairbanks, Alaska. American Journal of Epidemiology 108 (5): 377-385.

Knobeloch, L. (2002). Health effects of arsenic-contaminated drinking water. Final report. Wisconsin Department of Health and Family Services. Submitted to the Wisconsin Department of Natural Resources. Aug. 13, 2002.

National Research Council (1999). Arsenic in Drinking Water. National Academy Press, Washington.

Rahman, M.S., Hall, L.L., and Hughes, M.F. (1994). In vitro percutaneous absorption of sodium arsenate in B6C3F_1 mice. Toxicol. In Vitro 8: 441-448.

Smith, A.E. (2002). "Everything but the kitchen sink": Exposure to arsenic from bathing and other indirect pathways. Presented at: Arsenic in New England: A Multidisciplinary Scientific Conference. Manchester, N.H., May 29-31, 2002.

Wester, R.C., Maibach, H.I., Sedik, L., Melendres, J., and Wade, M. (1993). In vivo and in vitro percutaneous absorption and skin decontamination of arsenic from water and soil. Fund. and Appl. Toxicol. 20: 336-340.

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