A Step in the Wrong Direction on Arsenic

By ACSH Staff — October 12, 2004

According to a study in the August 2004 issue of Chemical Research in Toxicology, arsenic could be toxic at much lower levels than previously thought, raising the alarm that the new EPA drinking water standard of 10 parts per billion (ppb), to take effect in 2006, might still be too high.(1) But don’t dump the glass of tap water yet; the conclusions of this newest study were based on an in vitro study of a rat cell line.

While animal experiments play a crucial role in many fields of research, there has been much scientific debate about how heavily we can rely on high-dose, single-species animal tests as indicators of human toxins and carcinogens. Over-reliance on such studies as the basis for increasingly stringent regulations of various chemicals lacks scientific credibility and often results in unnecessary health scares. The scares draw energy and financial resources away from actual health dangers. The current study, conducted by researchers at Dartmouth Medical School, takes the issue of relying on animal tests another step in the wrong direction.

The term in vitro -- literally, "in glass" -- refers to any biological process that takes place in an artificial environment such as a Petri dish or a test tube. An essential part of medical research, in vitro procedures are most useful in the early or intermediate stages of experimentation to study the effects of a substance in isolation, without interference from natural bio-mechanisms involving hormones, enzymes, and immune responses. They have been used to understand mechanisms of toxicity, to identify cellular target sites of action, and to characterize cellular and molecular changes prompted by exposure to toxicants. They reduce variability, allow for greater control of the experimental environment, and are quicker and cheaper than their in vivo -- "in life" -- counterparts.

However, extrapolating in vitro results to whole animal situations -- even animals of the same species that provided the cell cultures -- has many limitations. These studies cannot take into account toxicant distribution in a whole organism, route of administration, or metabolism of the substance. Further, cells in culture are not exposed to circulatory, nervous, or endocrine system functions, or to the millions of cells, thousands of enzymes, hundreds of chemical messengers, and dozens of organs that work in concert within a whole organism. In other words, the biochemical processes leading from toxicant exposure to toxic effect in vivo are too complicated to be duplicated in vitro. This is very much the case when it comes to cancer formation, a multi-step process influenced by a variety of factors, many of which are still poorly understood. Therefore, making assumptions about cancer-causing substances in complex systems based on single-study data from isolated cell cultures is reductionist.

Couple all of this with the varied cellular mechanisms between different animal species, and it is easy to see why we should hesitate before altering chemical guidelines "at the drop of a rat."
Information derived from *in vitro* studies must be interpreted in the context of the whole animal, and the conclusions drawn should not too hastily be extrapolated to other species. Consider, if you will, the 1999 statement by the National Academy of Sciences: "Because of interspecies differences in the disposition of arsenic, more human studies are needed, including research using human tissues."(2) Even then, results must be replicable in multiple studies before drastic regulatory action is taken.

The Dartmouth study is unquestionably of value in that it indicates the specific action of low levels of arsenic on individual cells -- it acts as an endocrine disruptor *in those cells*. It does not immediately follow, however, without further study on human cells *in vitro*, as well as epidemiological evidence of *in vivo* human effects, that the new standard for arsenic in drinking water of 10ppb should immediately be reconsidered and lowered to 2-3ppb as Joshua Hamilton, professor of toxicology and pharmacology at Dartmouth and head of the study, seems to hope it will. And let us not forget the controversy that already surrounds the EPA decision to lower the maximum contaminant level (MCL) from 50 ppb to 10 ppb. Several studies have indicated that there isn’t ample epidemiological evidence to show 50 ppb causes adverse health effects in humans, much less 10 ppb.(3)

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