Assessing Human Health Risks from Arsenic Exposure using a Weight-of-Evidence Approach

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Abstract

The importance of considering a weight-of-evidence approach when evaluating the human health effects of arsenic at contaminated sites became clear during several recent projects involving potential impacts from mining operations. Elevated levels of arsenic were encountered in several Ontario communities, including one near a former gold mine, and one near a sintering plant. Risk assessments, involving multi-pathway exposure assessment (*i.e.*, air, water, soil, backyard produce, fish and market basket foods) and use of U.S. EPA slope factors revealed cancer risk levels in the 1-in-1,000 range. The Ontario Ministry of Environment (MOE) acceptable risk level is 1-in-1,000,000, and as a result these elevated risk estimates raised community concerns. Answers were needed to ensure public safety and satisfy community and regulatory concerns. Further investigation into the risk assessment revealed that: (i) market basket foods were the main contributor to arsenic-related risks; (ii) generic arsenic criteria in Ontario (*i.e.,* 25 ppm) result in elevated risk levels (*i.e.,* greater than 1-in-100,000); (iii) the contribution of soil to overall arsenic-related risks was small; all other pathways were less significant; (iv) health-based intervention levels, as determined by the risk assessment, proved to be economically and technologically impossible; and, (v) removal of all soil above the generic criteria would only result in a 2 to 4% reduction in overall risk.

It became clear that information beyond that typically contained within a standard risk assessment was required in order to facilitate the decision-making process. Therefore, limited health status studies were conducted which considered the incidences of cancer in the communities in question. In addition, urinary arsenic studies compared the potentially "impacted" communities with "control" (or non-impacted) communities. In all cases, these studies indicated that the impacted communities were similar to the control communities. Only after consideration of all lines of evidence (*i.e.*, risk assessment, community health status, and results of the urinary arsenic study) was it possible to conclude that elevated arsenic levels in both communities were not likely to result in adverse exposures or health effects to residents of the communities in question.

The Problem

The issue of the cancer potency of arsenic, and the interpretation of, and response to, predicted risks in excess of the traditional *de minimis* risk level of one-in-one-million has been a source of controversy and complication in the risk assessment and management of arsenic-contaminated media. Use of the U.S. EPA slope factors to estimate possible risks to people *via* all exposure pathways (*i.e.,* air, water, food, soils) results in high risk values from background (natural) sources (MOE, 1999; Fleming and Kuja, 1998). In Ontario, consideration of background soil levels (17 µg/g) and generic soil criteria (25 µg/g for residential land use), reveals risks in the one-in-one-hundred thousand range (MOE, 1997). This immediately results in problems explaining what such risk estimates mean. The unsatisfactory nature of these arguments relates to the discussion of potential health outcomes related to arsenic entering the environment from various human activities. To the human health risk assessor, the concern is not necessarily focussed on what risks are predicted for the specific population of study, but the risks relative to background or typical populations. In the case of arsenic, risks well above the *de minimis* level are routinely predicted for exposures associated with typical North American diets, and high-quality, regulated North American drinking water supplies. These problems were highlighted during several recent projects where elevated levels of arsenic were encountered in communities in Ontario, including one near a former gold mine in Eastern Ontario and one near a sintering plant in Northwestern Ontario. These elevated risk estimates raised concerns in the respective communities, and answers were needed to ensure public safety and satisfy community and regulatory concerns.

The Solution

To effectively communicate the apparently elevated risk levels related to arsenic exposures to the public can be highly problematic. As a result, the risk manager/communicator may require the use of additional tools in this process.

A Weight-of-Evidence Approach

A variety of "tools" such as risk assessment, bio-monitoring, predictive modelling and medical surveillance must be employed in order to capture the true context of arsenic-related health impacts (see Figure 1).

TOOL #1 Risk Assessment

A risk assessment comprises the evaluation of the potential for adverse health effects arising from exposures of receptors to chemicals present in the surrounding environment. Risk assessment procedures are based on the premise that the response of an individual to a chemical exposure increases in proportion to the chemical concentration in critical target tissues where adverse effects may occur. The concentrations of chemicals in the target tissues depend upon the degree of exposure, which is proportional to the chemical concentrations in the environment in which the individual resides.

TOOL #2 Biomonitoring

Biomonitoring, in these types of circumstances, involves measuring the concentration of arsenic in biological tissue, such as hair, fingernails, blood, or urine, from an exposed population.

A number of factors may influence estimates of arsenic exposure, making it difficult to attribute particular sources of arsenic contamination to measured arsenic concentrations in human tissues or fluids. Key confounding variables include (but are not limited to): age, geographic region, occupation and gender. Background sources of inorganic arsenic such as smoking, drinking water and consumption of a typical diet will significantly contribute to the total arsenic intake, and potentially, the total inorganic arsenic intake (Binder *et al*., 1987; Fleming and Kuja, 1998; Gradient Corporation, 1995; Hwang *et al*., 1996).

Biomonitoring - Urine

A significant advantage of using urinary arsenic as an indicator of exposure is the fact that the relationship between intake (or exposure level) and concentrations in the urine have been well-studied and validated (Gebel *et al*., 1998; Walker and Griffin, 1998). Studies of the excretion of inorganic arsenic and its metabolites subsequent to oral, dermal and inhalation exposure indicate that the majority of arsenic is excreted in the urine within a few days of exposure (Walker and Griffin, 1998).

However, to obtain an accurate reflection of the health risk related to these exposures, it is preferable to evaluate speciated arsenic, rather than total arsenic, as part of the risk assessment (Gebel *et al*., 1998; Walker and Griffin, 1998).

This detailed speciation is required as a result of the following:

- Total urinary arsenic measurements generally include all forms of arsenic (*i.e.*, As (III), As (V), monomethylarsonic acid (MMA), dimethylarsinic acid (DMA) and organoarsenic such as arsenobetaine and other trimethylated forms);

- The toxicity of arsenic is primarily associated with inorganic species, while organoarsenicals and trimethylated arsenic compounds are not considered to be relevant for toxicological risk assessments; and,

- Various studies have observed significant increases in total urinary arsenic levels after the consumption of seafood, however in general, have reported no significant increases in inorganic arsenic species (*i.e.,* As (III) and As (V)) or their associated metabolites (MMA and DMA).

As a result, speciated urinary arsenic is the recommended biomarker for recent environmental and/or occupational exposure to inorganic arsenic. It is important that the methods used by the analytical lab can distinguish between the non-toxic organoarsenicals and the toxicologically-relevant forms and their metabolites (As (III), As (V), MMA and DMA).

TOOL # 3 Predictive Modeling 0f Urinary Arsenic Concentrations

Predictive urinary arsenic modeling can be used to provide a comparison between biological monitoring data (*i.e*., urinary arsenic concentration) and predicted exposure estimates (µg/kg body weight/day) generated in the risk assessment (Walker and Griffin, 1998).

This comparison between predicted and measured values can then be used to refine the exposure assumptions employed in a site-specific exposure scenario, thereby calibrating the exposure models used to help predict human health risks.

TOOL #4 Medical Surveillance

The medical surveillance or health impact assessment tool can be defined as any combination of procedures or methods by which an area of elevated concentrations may be judged as to the effect(s) it may have on the health of a population.

It should be noted that health impact assessments can examine associated events beyond those specifically related to the health field (*i.e.,* economic, social, and environmental fields). Health is measured using a number of different tools, some of which are more directly based on the analysis of physical and biochemical endpoints. Other components of a health assessment require the development of interview instruments to evaluate public health initiatives. A study design for the impact assessment must be specifically developed for the community in question, and include a detailed rationale for each of the study components, a discussion of methodologies used in the study, and an analysis of the potential results and conclusions of the investigation.

Case Studies

In this review, two sites (communities in the vicinity of mining operations) located in Ontario, Canada, are presented.

Site 1 Former gold mine

- The gold-bearing ore was bound up with arsenic;
- The mine operated for about 50 years;
- Subsequent to closure, the site was used to process silver and cobalt ores from mines around the world;
- Pesticides were produced from the arsenic by-products of the smelting operations and continued as a major activity at the site until those products were replaced by organic pesticides in the late 1950s;
- A complex blend of toxic compounds, heavy metals and low-level radioactive wastes remained on the site with early clean-up efforts revealing serious contamination of the site's soil, surface water and groundwater;
- Near the mine site, over 1,000 soil, vegetation, water, dust, air samples were collected;
- Measured soil concentrations exceeded the regulatory clean-up guideline for arsenic at 123 of the sampled sites; and,
- The maximum concentration of arsenic detected was 605 µg/g (median=127 µg/g) compared to the Ontario soil cleanup guideline of 25 µg/g.

Site 2 A former iron ore sintering plant

- Arsenic was a contaminant of the raw ore used in the sintering plant;
- As a result of the ore processing, there were major stack emissions of arsenic;
- The plant was in operation for almost 60 years; and,
- Arsenic was the only contaminant of concern identified near the sintering plant.

By the time these two operations were shut down at both of these sites, many years worth of hazardous by-products and residues had built up on and around both sites, including residential areas near both sites, prompting the need for health risk studies in these communities.

Health Risk Studies

The purpose of the health risk studies was to answer the following questions:

- Are contaminants from the sites present in the community and if so, at what levels?
- What are the possible exposures that residents might have to the contaminants; how likely are these exposures?
- What are the possible health implications of exposures, if any?

An overview of the process used to conduct the health risk studies for both case study communities is provided below (also see Figure 2).

Evaluating the Weight of Evidence

The following elements were conducted as part of the *Weight-of-Evidence* approach to assess the health risks in each of these communities:

- Information beyond that typically contained in a risk assessment was required in order to facilitate the decision-making process;
- Limited health status studies were conducted which considered the incidences of cancer in the communities; and,
- Urinary arsenic studies compared the "impacted" and "control" communities

Risk Assessment

To evaluate the potential risk posed by arsenic to residents in these communities, fully stochastic multimedia human health risk assessments of the communities located near the sites were conducted. The resulting health risk estimates associated with exposure to inorganic arsenic were then compared to the exposure and risk estimates for typical Ontario residents. Results of these assessments indicated that:

- Although the mean arsenic soil concentration within the community was approximately 10 times the Ontario Typical Range, the assessment concluded that overall cancer risks as a result of exposure to inorganic arsenic were only marginally greater for residents of the 'impacted' sites (see Figure 3);
- Cancer risk levels (CRLs) for lung cancer associated with the inhalation of inorganic arsenic were insignificant relative to that of skin cancer;
- Greater than 99.5% of the total cancer risk was due to the risk of skin cancer;
- Up to 70% of the predicted skin cancer risks of community residents were the result of consuming general food basket items common to all Ontarians.
- The exposure pathway which had the greatest contribution to site-related risks was consumption of municipal drinking water (this may have been overestimated given the lack of availability of drinking water data and the method detection limit used at the time).

Biomonitoring: Urinary Arsenic Sampling

Evaluation of the total urinary arsenic data from community participants indicated a statistically significant increase in total urinary arsenic levels associated with those individuals who reported recent fish and/or seafood consumption (the focus of the analysis was confined to speciated urinary arsenic measurements as a bioindicator of recent inorganic arsenic exposure). However, statistical tests also revealed that there were no significant differences in both total and speciated urinary arsenic levels between residents of the "impacted" communities and the control groups (see Figure 4).

Furthermore, the measured urinary arsenic levels from the so-called "impacted" communities were below those measured levels reported in the published literature for communities near known point sources (MOE, 1999). In fact, the majority of speciated urinary arsenic samples fell below the method detection limit of 6 µg/L, which reaffirmed that during this "snap shot" in time (*i.e.*, 1 to 3 days prior to sampling), the populations of concern were not experiencing exposure to arsenic outside that of a typical "background" population. However, not knowing the actual concentration of this fraction of the population results in a high level of uncertainty associated with the statistical characterization of the measured urinary arsenic data set.

Calibration of the Multimedia Exposure Model Using Urinary Arsenic Measurements

To validate the exposure and urinary arsenic modelling, the measured values were also compared to the predicted concentrations (see Figure 5). The results of the urinary arsenic model showed good agreement with the measured concentrations for people living in the "impacted" communities and the "control" group.

Medical Surveillance

Limited medical surveillance studies were also conducted in each of the communities and involved the following activities:

- A review of cancer incidence and mortality rates in the impacted communities and the population in surrounding areas;

- A study of cancers (*e.g.*, lung, bladder, kidney, *etc.*) linked to arsenic exposures, and relatively common cancers which could provide useful comparisons; and,

- A special environmental health risk factor questionnaire, designed to examine possible relationships between arsenic levels in urine and different environmental factors (arsenic in soil and dusts, vegetable gardens, pesticide use, house pets, occupational exposure).

Results and Conclusions

While sampling of the various media indicated that there are elevated levels of arsenic in some localized areas of the communities, results of the studies indicated that:

- There was no statistical difference in levels of arsenic in urine between the "impacted" communities and the "control" (unexposed) communities;

- The levels of arsenic in urine in the "impacted" communities were not indicative of any excess levels of illness based on medical surveillance studies. Furthermore, the epidemiological review of cancer incidence and mortality data found that, for the cancers studied, no incidence or mortality rate was high enough to warrant more detailed analyses of the statistics;

- Estimated cancer risks from arsenic contamination are not measurably higher than those for typical Ontario residents;

- Overall predicted exposures and risks for arsenic were only slightly greater when compared to estimates for the typical Ontario resident;

- Market basket foods were the main contributor to arsenic-related risks for both the typical Ontario resident, and the typical "impacted" community resident; and,

- If all soils in the "impacted" communities were replaced with background soils, the overall risk would only be reduced by 2 to 4%.

It was concluded that there were no unsafe exposures or adverse health effects associated with the arsenic contamination found in the communities. As such, it may be necessary to consider all lines of evidence (*i.e.*, risk assessment, community health status, and urinary arsenic study) to properly evaluate whether elevated levels of arsenic pose health risks to residents living in an arsenic-impacted community.

References

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THE WEIGHT OF EVIDENCE APPROACH

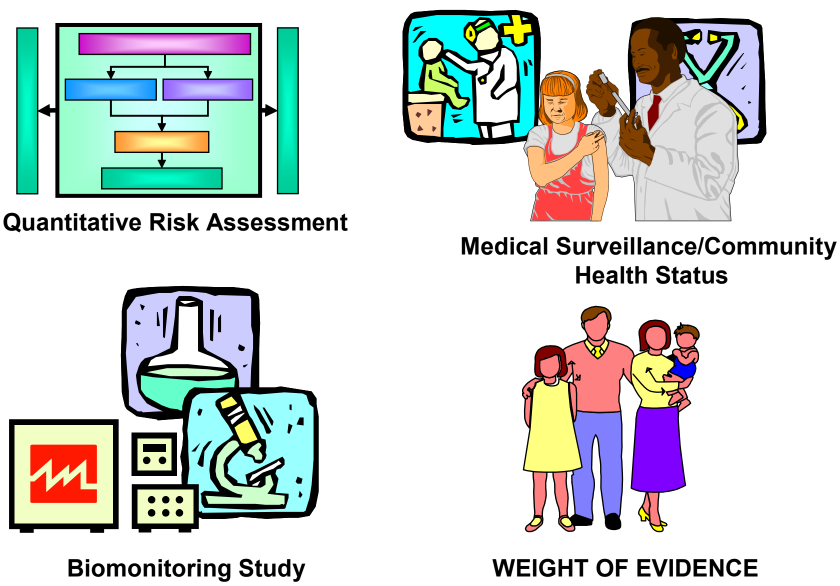

Figure 1 The Weight-of-Evidence Approach

THE HEALTH STUDIES

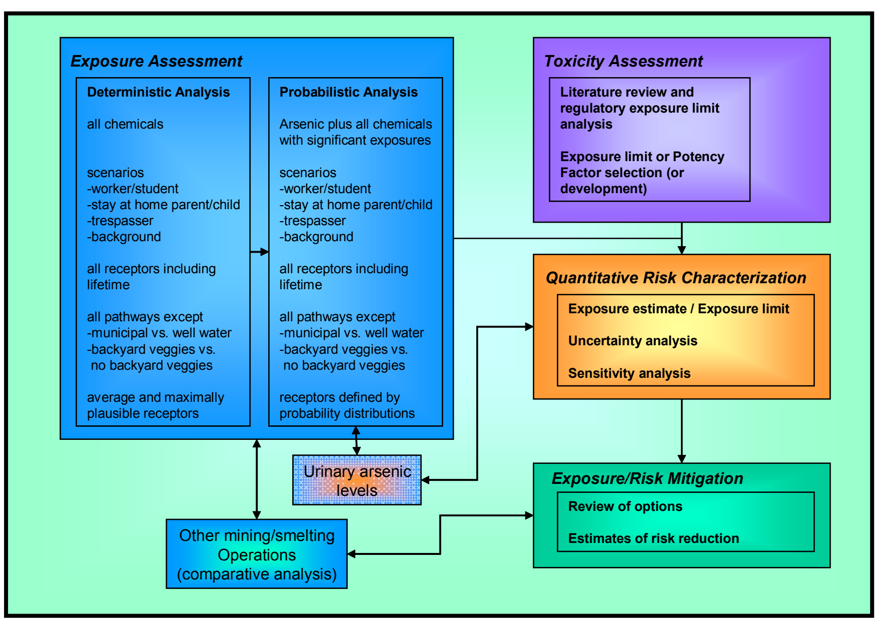

Figure 2 An Overview of the Health Study Process

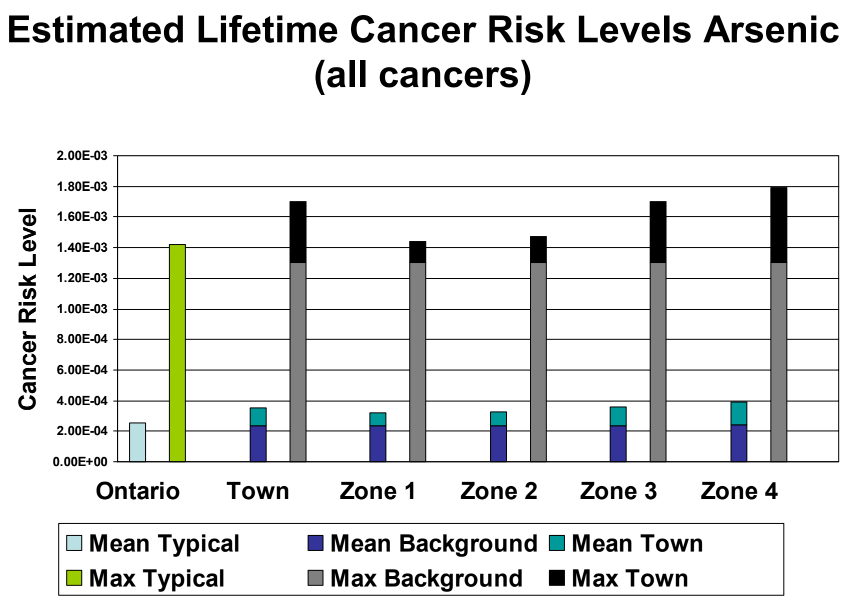

Figure 3 Estimated Lifetime Arsenic CRLs comparing the Community to Typical Ontario Background Risk

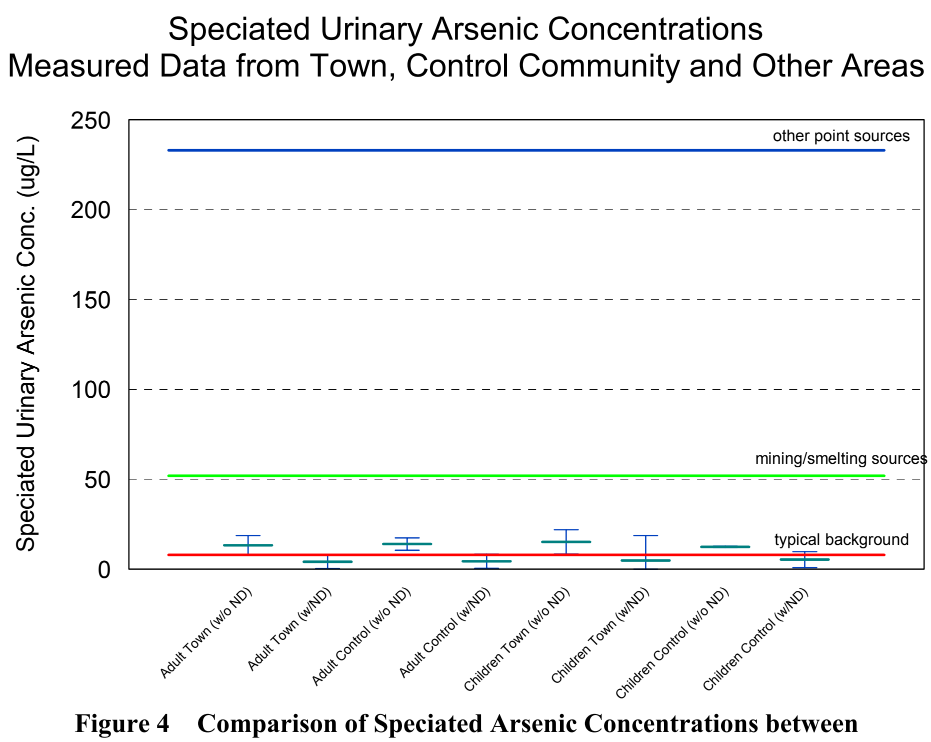

Figure 4 Comparison of Speciated Arsenic Concentrations between the Town and Control Communities

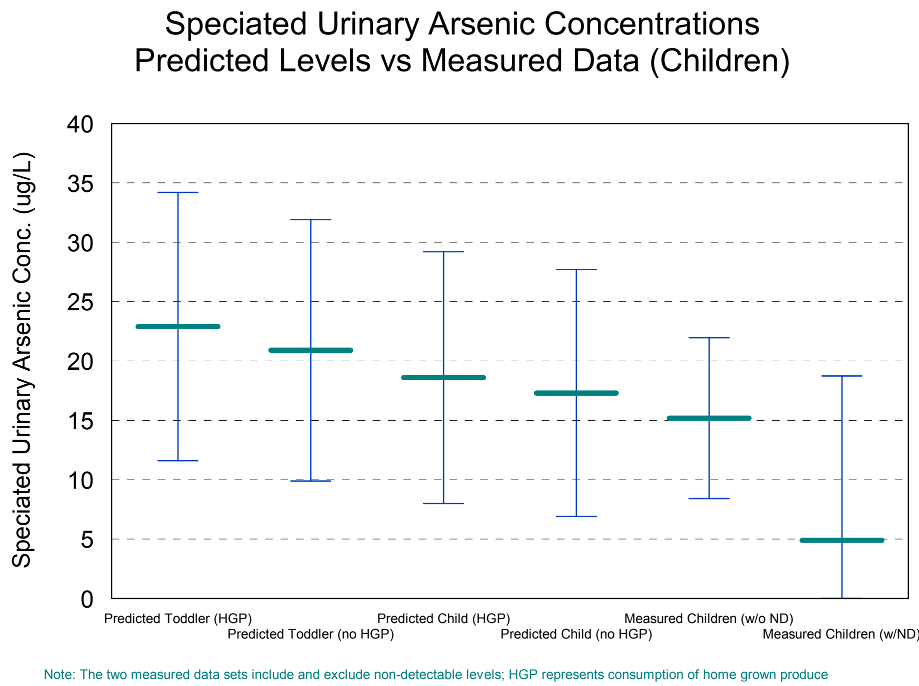

Figure 5 Comparison of Predicted *versus* Measured Concentrations of Urinary Arsenic in the Community