# Groundwater Contamination: Role of Health Sciences in Tackling

# 12

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**Abstract**

Groundwater contamination creates huge problems in many areas over the world. This chapter will use the arsenic contamination problem as a typical but the largest among such problems and discuss the importance of role of the health science or human biology for implementing sustainable, and especially small-scale, mitigation measures. Although the chapter will concentrate on arsenic, the chapter should have significant implications in considering not only other chemicals but also nonchemical (e.g., microbiological) contaminations.

Based on the authors' experiences in Bangladesh as well as on recent literature, the chapter will discuss the importance of dose-response relationship, a conventional component for risk assessment, focusing on (1) important modifying factors particularly associated with developing countries, where such problems are often encountered, and on (2) exposure evaluation. The chapter will discuss these two rather conventional issues under a new light and will try to show how the information from health science/human biological science can be utilized to devise adaptive approach in implementing engineering options.

Discussion of modifying factors including biological attributes (e.g., gender or genetics) and cultural/behavioral factors (as nutrition) will show that such modifying factors could pose substantial impacts on the dose-response relationship and will suggest such factors should be considered as an intrinsic part of the dose-response relationship rather than assuming a "universal" dose-response and its modifiers.

Discussion of exposure evaluation will include significance of non-water exposures and chemical speciation. The former will emphasize the exposure through food and may potentially lead to substantial revision of the mitigation measures, while the latter may show the practical importance of rapidly evolving

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scientific (toxicological/biological) knowledge in considering actual countermeasures. This portion, particularly the chemical speciation part, will be rather arsenic specific (as compared to the first discussion on the modifying factors) but still relevant to contamination by other chemicals.

As a whole, this chapter will try to demonstrate the importance of comprehensive biological/health science knowledge in implementing specific sustainable engineering measures.

## 1 Introduction

While provision of safe water is one of the most fundamental conditions for the sustainability of healthy population, more than one billion people throughout the world are still having a hard time to find appropriate water sources for daily living. As a result, diarrheal diseases presumably arising from poor water and sanitation are estimated to bring about 1.8 million deaths in 2002 (WHO 2006). Another estimation shows that water-associated diseases, including both those associated with unsafe water and those with poor sanitary facilities, account for 4% of total diseases burden in the world in terms of disability-adjusted living years, DALY (Young 2005).

It is estimated one-third of the world population is depending on groundwater (WHO 2006). While it is relatively free from biological (bacteriological) contamination compared to surface water is, chemical contamination occurs either due to chemicals migrating from the (soil) surface or leaching from the soils/rocks. Compared to biological (bacteriological) contamination, population at risk due to chemical contamination is less, but chemical contaminations, at least some of them, pose long-term and serious health effects such as cancer, which would hamper the sustainability of affected communities.

Arsenic is one of such chemicals and has been associated with the largest groundwater-associated chemical problems in the world. The problem has been mainly found in developing countries in Asia (including India, Bangladesh, Nepal, Vietnam, Thailand, Taiwan, and several regions in China) and Latin America (Peru, Argentina, and Chile), but it could account for substantial portion of waterborne outbreaks in developed countries such as USA (WHO 2006). In Japan, arsenic is one of the most frequently detected contaminants that affect the water quality of wells, only second to nitrite nitrogen, which is an indicator of biological (i.e., not chemical) contamination.

Since the arsenic contamination causes various health outcomes including serious ones, any solution of this problem should be compatible with reducing health risk to acceptable levels. To define this level, knowledge of health sciences will be required. While information is available regarding the risk associated with arsenic, this chapter will discuss some issues to be considered in delineating the risk and applying the risk knowledge, which would be also informative to tackle with similar problems with other type of hazardous chemicals.

## 2 A Brief Description of the Arsenic Contamination in Bangladesh

Bangladesh is a densely populated country with a total population of 150 million. Up to 1970s, the country depended on surface water for its drinking water, but due to the increase of human as well as livestock populations, biological (bacteriological) contamination of the surface water often led to outbreak of GI infections and became a big threat for the communities. By the end of 1970s, many tube wells were installed throughout the country under the guidance of the World Bank as well as UNICEF (Fig. 12.1), which eventually succeeded in drastically reducing the number of GI infection outbreaks. Thus, in the early period, the installation of the tube wells in Bangladesh was a success story.

The story began to change in early 1990s, when some odd diseases were observed in some area of Bangladesh, and in 1993, arsenic contained in the polluted tube well water was officially recognized as the causative agent. It was turned out that the arsenic in the groundwater comes from soil, thus is natural origin, although the mobilization of the soil-bound arsenic is associated with some anthropogenic process (Neuman et al. 2009). Despite many studies and governmental actions since then, currently, the country has the largest population at risk with regard to arsenic toxicity, which is estimated to be approximately one-third of its total population.

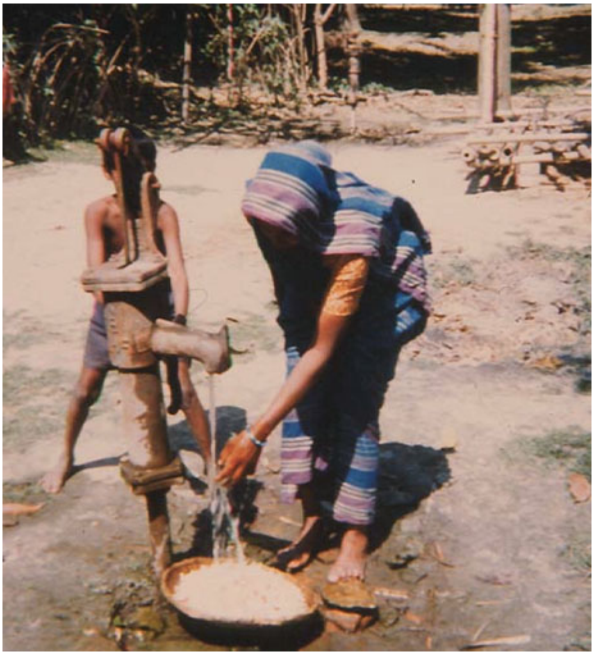


**Fig. 12.1** A tube well in a rural village in Bangladesh

Since more than 90% of Bangladeshi population are depending on groundwater as the sole source for the drinking water, to find out the appropriate way to tackle this problem is fundamental for the sustainability of the country.

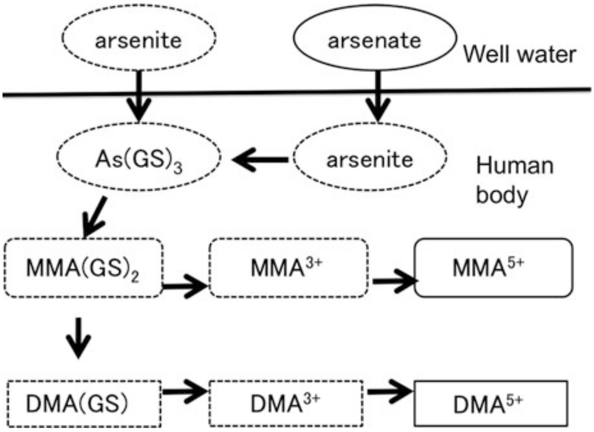
## 3 Toxicology and Health Risk Assessment of Inorganic Arsenic

### 3.1 Toxicology

While many chemical forms of arsenic exist, only arsenite and arsenate are the chemical forms found in contaminated groundwater. Effects of these toxic compounds vary with dose, and most of the groundwater contamination cases are associated with long-term, relatively mild extent of exposure, where "relatively mild" means that the dose would not lead to acute death. At this level, the most widely known effects are skin lesions, including keratosis in the palm and sole, and abnormal skin pigmentation – melanosis as well as leukomelanosis on the trunk. Effects on microcirculation are also known. The most serious consequence of such long-term, low-level exposure will be the development of the cancers of skin, kidney, bladder, and lung (even exposure through ingestion). Also, iAs is considered to be a risk factor for diabetes, hypertension and pulmonary diseases. Recently, several groups report neurological as well as developmental effects. Interested readers should consult with available reviews as already mentioned.

Arsenic found in the environment exists in a variety of chemical forms including both inorganic and organic ones. Arsenic compounds in groundwater exist as arsenite or arsenate, depending on the physicochemical condition of the water. Some marine organisms contain high amount of arsenic, which are usually in organic forms like arsenosugar, arsenolipids, or arsenobetaine. Forms in terrestrial organism (food) are also various with higher proportion of inorganic forms (EFSA 2009). Toxicity of the arsenic compounds reflects these differences in the chemical forms. Importantly, when ingested by human, the inorganic arsenic compounds undergo metabolic changes. The basic changes are described as methylation, but the metabolic pathway and its toxicological significance have been given new aspects in the last decade. Regarding the pathway, it has been assumed that the inorganic arsenics will be oxidatively methylated twice in the body, but this traditional scheme has been questioned recently by a report suggesting the involvement of glutathione in the methylation step (Fig. 12.2). Regarding the toxicological relevance of the metabolism, the whole process had been considered as detoxification process since the methylated forms showed much less toxicity in terms of lethality. Actually, trivalent methylated species (both for MMA and DMA) are found to be as toxic as and even more toxic than arsenite in some assay systems (Styblo et al. 2002). While the importance of the chemical forms and the metabolism will be described in later sections, it should be noted this is still an ongoing basic research issue.

**Fig. 12.2** Metabolic pathway of ingested inorganic arsenic. In the contaminated groundwater, most of arsenic exists as arsenate or arsenite, which are converted into organic forms in the human body after ingestion (GS = glutathione)



## 3.2 Risk Assessment

For many chemicals including arsenic, inorganic arsenic (iAs) to be exact, there are various useful sources, which provide health risk-associated information on the web. Many international and national organizations have been evaluating the health risk of iAs, and most of them has been updated time to time. In case of iAs, such organization includes, although not exhaustive, Integrated Risk Information System (IRIS) of EPA (USA), Toxicological Profile of ATSDR (USA), WHO Fact-sheet, IPCS-Environmental Health Criteria (IPCS 2001), IARC monographs, Joint WHO/FAO Expert Committee on Food Additives (JECFA 2010), and European Food Safety Authority. By consulting with these risk assessments, succinct answers to the question, “what is the level that is thought to be safe?,” may be obtained. Currently, EFSA (CONTAM Panel) concludes $BMDL_{1.0}$ values as ranging from 0.3 to 8 μg/kg bw/day, while US EPA indicates $BMDL_{0.5}$ 3.0 μg/kg bw/day. Both of these bodies indicate that the current Provisional Tolerable Weekly Intake of 15 μg/kg bw/week is not appropriate.

Most of the cases, these risk assessments are based on currently available and reliable information, collected under certain exclusion/inclusion criteria determined by each assessment body. The most sensitive and serious, serious in view of the health consequences, effects are identified, information providing doses-response relationship will be archived, and after considering the uncertainty of the information in various manner, the assessment will come to the final critical value, the definition of which varies one assessment/organization to the other. The procedure per se is quite well established, although it has been modified/changed according to the updated scientific knowledge. While final conclusion would sometimes differ among such assessments, reflecting the fluctuation of the knowledge bias, difference in the basic assumption of the dose-response models, or standpoint of committee (e.g., taking more precautious principle side or not), etc., these assessments provide a very good basis for taking or not taking any action on the real field.

While these procedures are well established, and most of the assumptions used in deriver process are explicitly shown, there are implicit assumptions that unevaluated or unmeasured parameters would not affect the assessment substantially. Generally speaking, for example, genetic differences and/or environmental differences are not taken into account at least in a quantitative manner, although they are sometimes mentioned. To rephrase, most of the assessments try to establish a universal assessment, at least in the past. This hidden assumption appears to be gradually changing recently. For example, summary from the 72nd meeting of JECFA (2010) pointed out that nutritional status as well as other lifestyle associated factors (although not identified so far) could be the sources of uncertainty. The recent EFSA evaluation (2009) concluded that skin lesions found in south Asian countries, long considered as the most common manifestation of the arsenic toxicity, may not be caused by iAs alone but caused by iAs combined with other factors like poor nutritional status; exposure to iAs is necessary but not sufficient condition to cause skin lesions.

For several reasons these issues should be taken seriously into the risk assessment in real world. First, including iAs problem, many of the sustainability problems are observed in developing countries, where many conditions including genetic make, nutritional status, coexistence of other environmental threats including hazardous chemicals, culturally specific behaviors (Bae et al. 2002) are different from those in the developed countries, where most of the "background" studies in the past risk assessments had been conducted. Second, compared to the past events like Minamata disease, most of the current risk issues are dealing with subtle health effects. This is exemplified by recent assessment of the health consequences of in utero methylmercury exposure on offspring. Sophisticated neurobehavioral test batteries (Grandjean et al. 1997) including Brazelton test (Suzuki et al. 2010) assessments could detect minute effects associated with low-level exposure to mercury. Third, which is also related with the second point, exposure would not occur with only a single chemical, usually exposure to multiple chemicals should be assumed regardless this fact should be incorporated in the assessment or not.

In the following sections, these issues will be considered in two approaches. The first one is to discuss the "modifiers" of iAs toxicity, which directly assess the issue, and the second one is to discuss the issue in terms of exposure. In the latter approach, it is hoped that the link between the exposure and these issues will be clarified along with the discussion.

## 4 Modifying Factors of Arsenic Toxicity

One of the prominent features of arsenic toxicity is the large variation of its manifestation both across populations and across individuals. In the field situation, there are sometimes households within which only some of the members are severely affected by arsenic, while other members are not at all, despite the fact that all members drink the water from the same source and share the food. Some researchers even think iAs may not be a sufficient factor of so-called arsenic symptoms (Mead 2005; EFSA 2009). There are a variety of candidate reasons why populations and individuals respond so differently with each other. These reasons could be either biological or social/environmental (Tseng 2009). Identifying such reasons may sometimes lead to elucidation of the toxic mechanism of arsenic. Although, often, classification into two (biological vs. social) might not be meaningful and even misleading, these will be discussed separately below for sake of discussion.

### 4.1 Biological Attributes

Effects of the age and sex have long been the targets of investigation in the risk assessment field. In case of arsenic, a clear sex differences have been described in many papers (Vahter 2007). The figure shows the sex difference in the prevalence of dermatological lesions induced by arsenic in Bangladesh and Nepal, where females show higher tolerance to arsenic toxicity than males do.

Mechanisms for the sex difference have not been elucidated. It has been known that difference in the water intake, behavioral difference like smoking, or alcoholic consumption cannot account for the sex difference. Hormonal effects should have the primary importance; other factors like sex-dimorphic brain structure or, nonbiological factors like differential intake of food (leading to differential nutritional status between sexes) or labor intensity may be among the candidates. Recently, it has been found that Bangladeshi women using estrogenic contraceptive exhibit suppressed iAs-induced oxidative stress compared to their non-contraceptive counterpart (Sultana, unpublished).

While these studies suggest the importance of sex hormones (or estrogenic activity), it awaits further confirmations. If such mechanisms will be identified, this could lead to a development of the “antidote.” One of such candidate mechanisms is associated with the metabolism of the ingested iAs. It has been known that ingested iAs will undergo a series of metabolic changes, where the compound will get methylated twice (Fig. 12.2). The metabolic change was understood as a detoxifying pathway since injection of the resultant methylated species revealed much less toxicity compared to the “parent” iAs species. This long held view has been challenged and eventually changed during the last decade; it has been found that an intermediate species mono-methylated, trivalent arsenic (As(III)) are as much toxic as the parent iAs like arsenate in a variety of experimental assays. The methylation status can be inferred by examining the urinary profile of the excreted arsenic species using HPLC-ICP-MS system, which will be described later.

Finally, it should be noted that although the sex difference in skin lesions, i.e., higher susceptibility of males, have been reported by many researchers, this may not be the case for some other endpoints. For example, in arsenic polluted area in the Terai region, the lowland Nepal, a negative correlation between the arsenic intake level and BMI, an indicator of general nutritional status (presumably reflecting energy balance) was found (Maharjan et al. 2007). While there were sex difference in terms of skin lesions, no sex difference was found in the BMI suppression.

Interaction between the genetic make up vs. environmental factors become one of the hot fields in the environmental health sciences. Since above-described metabolism of iAs contains some enzymatic processes, researchers focused on

**Table 12.1** Some of the genetic polymorphism potentially associated with metabolism or toxicity of inorganic arsenic

| Polymorphism | Effects | Reference |
|---|---|---|
| Arsenic methyltransferase | Associated with metabolism, cancer risk, or with DNA damage | Engstrom et al. (2011), Sampayo-Reyes (2010), Agusa et al. (2009), and Fujihara et al. (2009) |
| Glutathione S-transferase M1 | Deletion may be associated with modified metabolism | Ghosh (2006) and MacCarty et al. (2007) |
| Glutathione S-transferase T1 | Deletion associated with higher body burden; but, increased risk | Kile et al. (2005) and MacCarty et al. (2007) |
| Purine nucleoside phosphorylase | Increased sensitivity to skin lesions | De Chaudhuri et al. (2008) |
| XRCC3 | Protection against skin lesions associated with polymorphism | Kundu et al. (2011) |
| Heme oxygenase-1 | Shorter GT repeat may be associated with reduced risk for cardiovascular mortality | Wu et al. (2010) |
| Cystathionine-$\beta$-synthase | Some SNPs associated with metabolism | Porter et al. (2010) |

genes coding for such enzymes as methyltransferase or glutathione transferase isozymes, while others chose other proteins. Table 12.1 shows the examples of such genetic variants and their relationship with the toxicity. Basically, such measurements per se are simple and hence could be carried out without many difficulties. On the other hand, choice of the samples and interpretation of the results need much more attention. Statistically derived relationship between polymorphism and arsenic toxicity is still being accumulated, and the hypothesis should be re-evaluated with more samples. As in the case of the susceptibility against multifactorial diseases, it is obvious that more than one gene will be involved in modifying the toxic consequences. A genome-wide explorative approach to identify the potential genetic influences is an unexplored and promising way.

## 4.2 Environmental/Cultural Attributes

People are never exposed to a single chemical. They are immersed in "environment," which means they are exposed, not only to iAs, the chemical of concern, but also to numerous environmental biophysical and social factors. It is natural that consequence of the iAs exposure would be different under different environmental settings/parameters. For example, the absorption of cadmium or lead is depending on the iron nutrition of the person presumably due to the competition between the iron and these elements (Kordas et al. 2007). Investigation of such interaction among numerous factors is, however, impractical, and investigator needs to focus on most relevant variables. Currently, this focusing task is "handmade," i.e., conducted empirically, and there is no systematic procedure to do this. Investigators need to arbitrary choose potentially relevant factors based on his/her knowledge on the biological mechanisms as well as the feasibility of data collection. Considering the complexity of the exposure and subtleness of the outcomes, which most of the environmental health issues are sharing, systematizing this step is an urgent task, although it is not an easy one.

One would implicitly assume that toxicity of chemicals is exaggerated when the nutritional status of the host organism is poor. While this sounds as trivial, epidemiological evidence is scarce (Li et al. 2008). It has been shown in a Nepali lowland population that those having smaller BMI, less than 18.5, show higher prevalence of skin lesions at the same level of the exposure (Maharjan et al. 2007). In a separate report in Latin America, nutritional status for several nutrients, each altered the toxicity up to two folds in terms of odds ratio for developing skin lesions (Mitra et al. 2004). This kind of observations have much practical implication since many of environmental hazardous are found in developing countries, where poor nutritional status would be often expected.

Sometimes behaviors, customs, or habit that are specific to a particular culture/population may influence the toxicity. In some part of Bangladesh, rice is cooked in a pot with a plenty of water. After cooking, excess amount of water is discarded. If the water is contaminated by arsenic, this cooking process will increase the concentration of arsenic in the cooked rice. In this case, the ratio of water to rice would affect the final arsenic content of the rice; when they cook the rice in their local style (with a large excess of water), arsenic dissolved in the water will be condensed into rice grain during this cooking.

The cases discussed in this section highlight the importance of “modifying” factors. The use of the term “modify” reflects the fact that the focus here is arsenic and other factors are “side players,” which in turn reflects the assumption that there is something like a “universal” or “true” dose-response relationship that would be modified by many confounders. In fact, toxicity emerges under various environmental settings, and there is no “standard” condition against which the “universal” toxicity should emerge. Such consideration has been gradually emerging in the risk assessment scenes. A recent example of this is risk assessment in methylmercury contained in fish (that are not “artificially” contaminated as in the case of Minamata disease). The neurobehavioral toxicity of methylmercury emerges only when nutritional factors are taken into the statistical model. This fact implies that the toxicity would depend on nutritional status of the population (Rice 2008). In case of genetic influences, lack of standard condition is more apparent, since there would not be a standard set of genome. Considering the number of genes that could modify the toxicity, it would be more appropriate to regard toxicity as a function of aggregated set of genotypes rather than an imaginary universal toxicity modified by numerous variant of each relevant gene. In addition, the presence of other hazardous, sometimes even unidentified, chemicals may increase the complexity. Recent EFSA evaluation (2009) concluded that arsenic is not a sufficient condition for the skin lesion observed in Asian countries; it should be more appropriate to consider the skin lesions as an integrated toxicity of arsenic combined with some unidentified conditions/factors. Simply, it is not known what kind of condition is required for other symptoms observed in other regions.

## 5 Evaluating Exposure

The exposure status needs to be examined to decide whether the situation needs some intervening actions or policy implementations. While the established dose-responses relationship and health risk assessment are given in the form of abstract information, exposure evaluation reflects regional specificity and local context. A good reference for arsenic exposure in general population can be found in a nationwide survey conducted in USA, which also provides information about chemical forms of arsenic (Centers for Disease Control and Prevention 2009).

### 5.1 Potential Importance of the Non-water Sources

Since arsenic contaminates the groundwater, most of the attention has been paid to iAs in the water sources. Also, most of the epidemiological studies have used the iAs concentration (multiplied by water intake, in some cases) in groundwater as dose indicator. Here, examined was the relationship between urinary arsenic concentration, a frequently used good indicator of exposure, and iAs concentration in the well water. When whole range of the dose was examined, the two indicators show a good correlation as expected, but they show deviation in the lower end of the dose ranges (Fig. 12.3). Such deviation suggests there are sources of iAs other than the groundwater. A calculation based on some limited number of food samples show substantial amount of arsenic come from food items. If it is assumed that the arsenic contained in the food items are predominantly iAs, then the amount in the food will exceed the Provisional Tolerable Weekly Intake (PTWI) (Watanabe et al. 2004).

In fact, arsenic contained in the food items exists in a variety of chemical forms. Based on an extensive survey of food arsenic measurement, the EFSA concluded that overall estimate of the proportion of iAs against total arsenic is 70%, ranging from 50% to 100% (EFSA 2009). Seafood has much lower proportion of iAs compared to the terrestrial species. While fish and marine organism contain high concentrations of arsenic, less toxic chemical forms like arsenobetaine is predominating (Borak and Hosgood 2007). Among the marine organisms, however, *hijiki*, marine algae, is unique in that it contains high proportion of iAs, which might pose non-negligible cancer risk on *hijiki*-consuming Japanese population (Nakamura et al. 2008). Therefore, it should be kept in mind that the proportion of iAs varies considerably depending on the food types.

Most of the mitigation attempt has been focusing on the removal or arsenic from water sources or changing water sources per se. To reduce the exposure is important, but current strategies restricted to water arsenic might not be enough, and additional strategy to reduce arsenic intake from food might be required. At this point, there are missing information including the speciation of arsenic and the origin of arsenic

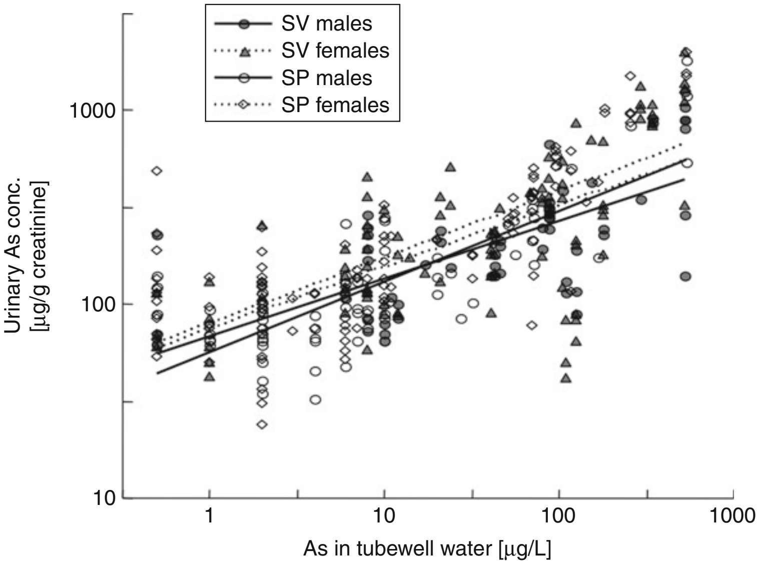


**Fig. 12.3** Correlation between the urinary concentrations of arsenic of residents living in arsenic-polluted area (*vertical*) and concentrations of arsenic in the respective well water used by these residents (*horizontal*). Note both axis are drawn in logarithmic scale

in various food items. The latter, the origin of arsenic, will be related with the environmental behavior of arsenic and mechanism of mobilization of arsenic from soil (e.g., see Neuman et al. 2009).

## 5.2 Media for Exposure Evaluation

There are two approaches to evaluate the exposure: environmental monitoring and biological monitoring. While the former relies on the amount of the (hazardous) materials of concern in any environmental media including air, water, food, and even soil, the latter uses "biological media" such as blood (whole blood, plasma, or serum), urine, saliva, hair, nail, and breast milk. The relative usefulness and appropriateness of each medium vary according to the purpose of the evaluation and substance of concern (Table 12.2). In case of multimedia exposure, where the exposure occurs through more than one route, the biological monitoring will provide easier way for quantifying the individual exposure, while it cannot pinpoint the major source of exposure that needs to be regulated. In so-called arsenic polluted areas, while majority of exposure occurs through ingestion of contaminated groundwater, exposure through the food items may not be negligible as discussed above. Therefore, accurate quantification of exposure requires exhaustive quantification of both arsenic in major food items and amount of food consumed, which is labor taking and virtually impossible in most of the field situation.

**Table 12.2** Biological media commonly used for biomonitoring of hazardous chemicals

| Medium | Invasiveness | Handling | Storage/transportation | Others |
|---|---|---|---|---|
| Blood | Large | Infection risk | Infection risk | Rich information. Blood cells and serum will give different type of information |
| Urine | Little | | Degraded if left | Not appropriate for lipophilic substances. Effect of dilution and condensation |
| Hair | Very little | Easy | Easy | External contamination |
| Saliva | Little | | Infection risk | Relatively scarce information |

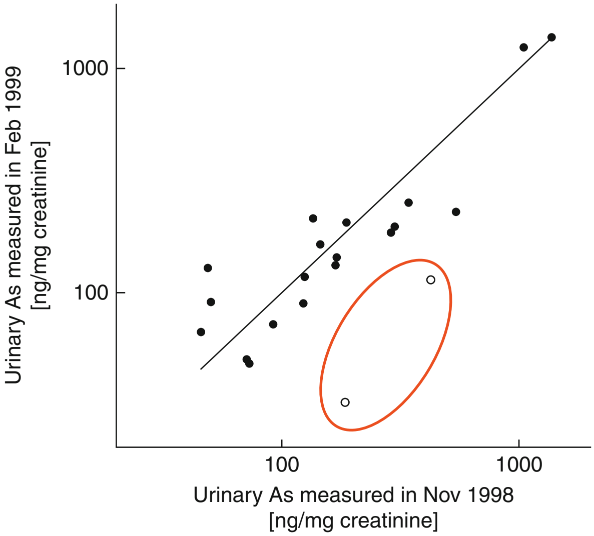


**Fig. 12.4** Correlation between two urinary arsenic measurements from the same group of individuals sampled with a 3-month interval. Only two persons that changed their water sources showed apparent discrepancy between two period

There is no known biological media that reflects longer (cumulative) exposure to arsenic. Biological monitoring of arsenic usually relies on urinary arsenic because of its relative accuracy in reflecting arsenic intake and relative ease in field sampling. Another advantage of urine sample is that it can provide information about arsenic metabolism if the sample is appropriately stored and analyzed with devices capable of chemical speciation, for example, HPLC-ICP-MS. In the field setting, so-called spot urine sample is taken as the surrogate for the cumulative urine (e.g., a 24-h urine sample). Urine is better than blood arsenic in that it has longer biological half-life, which is, however, only a couple of days. In a relatively homogenous food consumption pattern in rural Bangladesh, urinary arsenic concentrations in the pairs of samples collected from the same group of individuals with a 3-month interval show remarkable consistency. The only two exceptional individuals were those who switched from their former contaminated wells to newly installed virtually noncontaminated wells between the two sampling periods (Fig. 12.4). Thus, this simple scattergram provides some hints for the chronological aspect of urinary arsenic.

## 6 Importance of Identifying Chemical Species

The urinary excretion profile as revealed by HPLC-ICP-MS provides information on the metabolism of ingested arsenic in the body as well as the chemical form of the arsenic ingested. For example, the excretion profile of Japanese and Bangladeshi people are quite different; Japanese urine contains relatively high amount of arsenic, most of which is accounted for by the presence of seafood-derived organic arsenicals (mainly arsenobetaine), which is considered to be much less toxic than iAs. On the other hand, the profile from an arsenic-polluted area in Bangladesh residents consists of arsenite, arsenate, monomethylarsonic acid (MMA), and dimethylarsinic acid (DMA). Regarding this profile, several researchers report that when the proportion of MMA (mono-methylated species) against the total arsenic increases, toxicity of the arsenic is enhanced (Valenzuela et al. 2005). It is noteworthy that the excretion profile shows a sex difference, where males have a higher proportion of MMA compared to females do; this observation appears to be consistent with the fact that males are more sensitive to arsenic toxicity. It has been also pointed out that in a northern Argentina population, proportion of MMA are found to be quite low compared to other population and that this abnormal excretion pattern may be evidence of genetic adaptation (Vahter et al. 1995), since the population in this area have resided the same place for a long period, which is different from the situation in the South Asian countries. Although this hypothesis needs to be tested, this could be an example, in which toxicity of certain chemical depends on the past history of the population.

Thus, the chemical speciation of arsenic is crucial not only in elucidating the mechanisms of differential susceptibility but also in the evaluation of exposure. Clearly, much effort should be made to fill the knowledge gaps in this field. Depending on the newly emerging knowledge, the mitigation measure might be substantially modified.

## 7 Summary

Established risk assessment as appeared in many national as well as international agencies carries neat message relating critical toxic effects with certain expression of doses. This standard dose-response relationship is actually assuming that the background information provided by the background studies would represent average human responses to the toxicant. In the field settings, where sustainability is the issue, variety of factors affects the manifestation of toxicity. Since most of the case, what is observed in an individual or population is an integrated effect of numerous environmental factors, it would be better expressed as the function of multiple variables. In this connection, the toxicity should vary according to the population and regions. Likewise, exposure is intrinsically a local phenomenon, which needs close examination to be quantified, and the combination of environmental and biological monitoring will make the most meaningful tool.

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