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REVIEW

Arsenic geochemistry of groundwater in Southeast Asia

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Abstract **The occurrence of high concentrations of arsenic in the groundwater of the Southeast Asia region has received much attention in the past decade. This study presents an overview of the arsenic contamination problems in Vietnam, Cambodia, Lao People's Democratic Republic and Thailand. Most groundwater used as a source of drinking water in rural areas has been found to be contaminated with arsenic exceeding the WHO drinking water guideline of 10 μg·L^{-1}. With the exception of Thailand, groundwater was found to be contaminated with naturally occurring arsenic in the region. Interestingly, high arsenic concentrations (> 10 μg·L^{-1}) were generally found in the floodplain areas located along the Mekong River. The source of elevated arsenic concentrations in groundwater is thought to be the release of arsenic from river sediments under highly reducing conditions. In Thailand, arsenic has never been found naturally in groundwater, but originates from tin mining activities. More than 10 million residents in Southeast Asia are estimated to be at risk from consuming arsenic-contaminated groundwater. In Southeast Asia, groundwater has been found to be a significant source of daily inorganic arsenic intake in humans. A positive correlation between groundwater arsenic concentration and arsenic concentration in human hair has been observed in Cambodia and Vietnam. A substantial knowledge gap exists between the epidemiology of arsenicosis and its impact on human health. More collaborative studies particularly on the scope of public health and its epidemiology are needed to conduct to fulfill the knowledge gaps of As as well as to enhance the operational responses to As issue in Southeast Asian countries.**

Keywords arsenic; groundwater; drinking water; arsenicosis; Mekong River; Southeast Asia

Introduction

Sustainable access to safe drinking water is one of the key Millennium Development Goals (MDGs) proposed by the United Nations. In particular, accelerated and targeted efforts are needed to bring drinking water to all rural households. Groundwater resources, which constitute approximately 97 percent of global freshwater [1], are an important source of household water consumption in many parts of the world, especially in rural areas. Groundwater is usually preferred as a source of drinking water due to its naturally stable state of microbial quality [1,2]. However, in some cases, naturally occurring chemical constituents in groundwater have been reported to pose significant risks to human health. The natural occurrence of arsenic in groundwater constitutes a setback in the provision of safe drinking water to millions of people in Asia [3]. Arsenic (As) is a toxic element classified as a human carcinogen that contributes to cancers of both skin and internal organs (liver, bladder, kidney and intestinal) [4]. Arsenic was detected in groundwater for the first time in the early 1990s in Bangladesh and West Bengal of India. It has now also been detected in several parts of China, Nepal and Pakistan and most Southeast Asian countries including Cambodia, Vietnam, Myanmar, Lao People's Democratic Republic (Lao PDR), Thailand and Indonesia [3,5]. According to an estimate by the World Bank, approximately 60 million people in South and East Asia are at risk from high levels of naturally occurring As in groundwater, with many people still drinking As-contaminated water on a daily basis [3]. Moreover, at least 700 000 people have been affected by arsenicosis, especially in rural areas. Even though a number of review articles have been published on As-contaminated groundwater around the globe, there is still a significant dearth of knowledge relating to As contamination of

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groundwater in Southeast Asia (SEA). Therefore, the focus of this review is the current knowledge on As contamination of groundwater in the SEA region, especially the public health aspects of groundwater protection as a component of an integrated approach to drinking water safety management. Additionally, the most recent case studies on As contamination of groundwater conducted by the International Environmental Analysis and Education Center (formerly known as the International Environmental Research Center) over several areas of Vietnam, Cambodia, Lao PDR and Thailand are discussed.

Background of arsenic contamination in groundwater and its health effects on humans

Worldwide distribution of arsenic groundwater contamination

The concentration of As in groundwater is typically below the World Health Organization (WHO) guideline for As in drinking water of 10 $\mu g \cdot L^{-1}$ [3,7]. However, a number of large aquifers with As naturally occurring at concentrations greater than 10 $\mu g \cdot L^{-1}$ or even significantly higher have been identified in several parts of the world [3,6]. Fig. 1 shows the distribution of globally documented cases of naturally-occurring As groundwater contamination, which is particularly high in parts of Argentina, Bangladesh, Chile, China, Hungary, India, Lao PDR, Mexico, Myanmar, Nepal, Pakistan, Romania and Vietnam as well as many southwestern parts of the USA [3,5,6]. Some of the better documented cases of naturally-occurring As groundwater contamination have been reported by Smedley and Kinniburgh [6] as well as Rahman *et al*. [5]. In contrast to the problems associated with As from mining and geothermal activities, which are generally localized, the occurrences of As in major aquifers usually occupy large areas [6]. Thus, such naturally-occuring As groundwater contamination may be potentially much more serious than local As contamination from mining or geothermal activities, since major aquifers typically provide drinking water to large populations. Generally, As mobilization in groundwater can only exist under specific circumstances, which are mainly related to the geochemical environment as well as the past and present hydrogeological conditions in the area [3,6]. Moreover, a high concentration of As in groundwater is not necessarily related to areas with high As concentration in source rocks [6].

Mechanisms of arsenic mobilization

As shows high sensitivity to mobilization at the pH values typically found in groundwater (pH 6.5 to 8.5), under both reducing and oxidizing groundwater conditions [1] and can also occur in both humid and arid climates [6]. The mobilization of As can also be favored by biotic and abiotic processes [8].

Fig. 1 Distribution of globally documented naturally-occurring As groundwater contamination (Modified after References 2, 3, 5, 6)

Reducing environments

The mobilization of As under reducing conditions is usually found in recently-deposited fine-grained deltaic and alluvial sediments [3]. The aquifer sediments derived from river systems are generally capped by a layer of clay or silt, which effectively restricts the entry of air to the aquifers [6]. In the presence of degradable organic carbon (solid organic matter) deposited with sediments, highly reducing (anaerobic) conditions develop [3,6,8]. These highly reducing conditions favor desorption of As from the mineral sources in aquifer sediments. The most important mineral sources in aquifers are metal oxides (especially Fe oxides) and sulfide minerals (especially pyrite) [3]. The reduction of solid-phase As to As(III), desorption of As from Fe oxides (As-bearing Fe(III) oxides), reductive dissolution of the oxides themselves and expected changes in Fe-oxide structures as well as their surface properties follow the onset of the reducing conditions [3,6,8,9]. In such cases, anaerobic metal-reducing bacteria can play a key role in the mobilization of As in sediments [6,10]. Therefore, the nature (type and availability) of organic matter plays a key role in controlling the activity of the microbial community and the subsequent rate of any geochemical processes [6,10]. Moreover, it has been found that the capacity for the release of As is severely limited by the availability of electron donors in the sediments [8]. Several investigations have revealed that increased As content in groundwater is well-correlated with several factors such as areal and vertical distributions of peat deposits, the degradation of which is the major redox controller, the redox driver in the groundwater system, groundwater movement [9], pH, HCO_3^-, Fe, Mn, and Al oxides and dissolved organic carbon (DOC) concentrations of sediments [11] as well as grain size [11,12]. As leaches out very strongly from sediments rich in $NaHCO_3$ and those with high pH [11]. This type of As mobilization has generally been reported in Quaternary aquifers in South and East Asia [3,6].

Oxidizing environments

As can also be released under oxidizing (aerobic) conditions, where the groundwater pH varies from acidic to basic conditions [3,6]. This tends to occur in arid and semi-arid areas as a result of extensive mineral reactions and evaporation. Groundwater with high As concentration is found in some arid inland basins in the western USA, Mexico and Argentina [3,6]. Since the environment is arid in those areas, evaporation is the reason for the positive correlation between As concentration and high B, F, Mo, F, V, HCO_3^- levels, and salinity. Under arid conditions, silicate and carbonate weathering reactions are pronounced and consequently, the groundwater often has high pH. Under oxidizing and high pH conditions, metal oxides in sediments (particularly Fe and Mn oxides and hydroxides) are expected to be the main source of As desorption under high pH conditions [6].

Metabolism of arsenic

Extensive biotransformation of As occurs after the ingested inorganic As (both As(III) and As(V)) enters the cell [13]. Metabolism of inorganic As occurs through a sequence of reactions, as illustrated in Fig. 2 [13–16]. In brief, inorganic As is enzymatically converted to methylated products, i.e. monomethyl arsenic (MMAs) and dimethyl arsenic (DMAs). Finally, biotransformation of inorganic As results in the presence of inorganic, mono- and dimethylated arsenicals in urine [13]. The human body can absorb, process and excrete about 40% to 70% of the total ingested inorganic As dose within 48 h [16].

As shown in Fig. 2, As usually occurs in two oxidation states (III and V). Once absorbed, As(V) is reduced to As(III), mainly in the blood and liver [16]. The As(III) is then taken up by cells and oxidatively methylated from As(III) to methylated As(V)-containing products. Thereafter, As in the methylated products is reduced from As(V) to As(III) before the next round of methylation. Thus, the coupling of oxidative methylation and arsenate reduction in As metabolism has a striking effect on the distribution and clearance of this metalloid [13]. The reduction of As(V) can be accomplished by the concurrent chemical oxidation of a thiol-containing molecule (such as glutathione) [14,15]. In addition, several enzymes, including purine nucleoside phosphorylase, function as As(V) reductases [15]. S-adenosylmethionine-dependent methyltransferase (methyl donor) catalyzes the

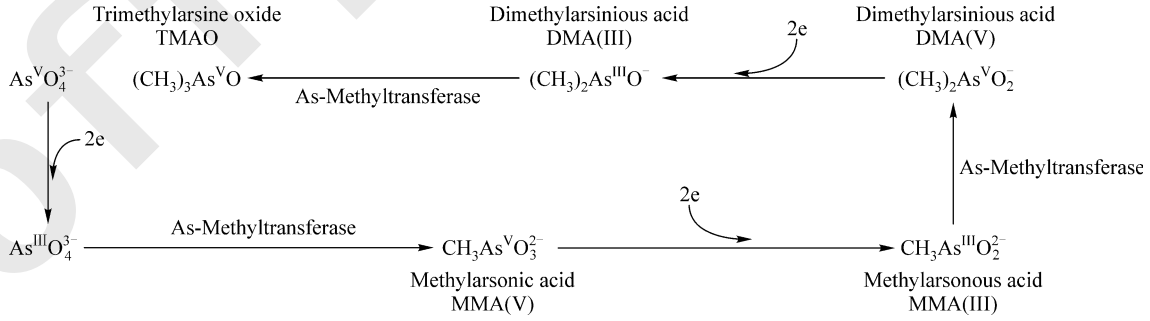

Fig. 2 The metabolism of inorganic As (Modified after References 13–16).

formation of MMAs and DMAs from As. Generally, arsenicals that contain As(III) are the preferred substrates for enzymatically catalyzed methylation. Therefore, MMA(III) [15–17] and DMA(III) [18] are the intermediates in the metabolic pathway and the obligatory substrates for the second and third methylation reactions that yield DMA and trimethylarsine oxide (TMAO), respectively. TMAO is found at very low concentrations in human urine. Rats are the only species that excrete significant amounts of TMAO [16].

(Bio)methylation of As has been generally considered a primary detoxification mechanism [14,15,17]. However, trivalent methylated arsenicals (such as, MMA(III) and DMA(III)) have been detected in the urine of subjects chronically exposed to drinking water containing high levels of inorganic As [14–16]. These trivalent arsenical intermediates are highly reactive and more carcinogenic than pentavalent arsenical intermediates [14]. Therefore, methylation of As can also be considered an activation process.

Toxicity of As to humans

As has no known physiologic and biochemical function in any living organism, including humans [17]. The toxicity of As to humans largely depends on the chemical form and physical state of the compound involved [7]. Even though As can occur in the environment in several oxidation states, inorganic oxyanion forms such as arsenite (As(III)) and arsenate (As(V)) are mostly found in natural waters [1]. As (III) is generally regarded as being more acutely toxic than As (V). Jomova *et al*. [14] have reported that the majority of As that enters the body is As(III) and it does so via a simple diffusion mechanism, while As(V) crosses cell membranes via an energy-dependent transport system. Similar to other toxic metals, the most potentially toxic forms of As are converted to less toxic forms in the human body. Finally, As is then excreted from the cell since it lacks biomagnification properties [17]. Dose [14] and host factors such as, individual susceptibility to As [14], sex [15], age [14,15], nutritional status [7,15,19], health status and lifestyle [13] of affected individuals are the major factors affecting the extent of damage caused by As poisoning.

Trivalent arsenic toxicity

As reported by Jomova *et al*. [14] and Hughes [18], the inhibition of numerous cellular enzymes caused by trivalent inorganic As (As(III)), such as pyruvate dehydrogenase, through thiol and vicinal sulfydryl group binding leads to the prohibition of the important biochemical processes and could then lead to toxicity; for example, the reduction in acetyl coenzyme A (CoA) and cellular ATP production as well as the activity of the citric acid cycle. Moreover, trivalent inorganic As can also inhibit the production of glutathione, which protects cells against oxidative damage [14].

Methylated trivalent arsenicals, such as MMA(III), are potent inhibitors of glutathione (GSH) reductase and thioredoxin reductase. The inhibition of these enzymes results in an altered cellular redox status and eventually leads to cytotoxicity. Both inorganic and organic trivalent arsenicals have also shown indirect genotoxicities *in vitro* [16]. Khan and Ho [20] reported that MMA(III) is the most potent inhibitor of DNA repair. The activities of methylated trivalent arsenicals are greater than those of trivalent inorganic As (As(III)), MMA(V), and DMA(V) [18].

Pentavalent arsenic toxicity

The toxicity of pentavalent inorganic As (As(V)) is due to its conversion to trivalent As, from which the toxic effects proceed as summarized earlier. More specifically, pentavalent inorganic As, which has a similar structure to that of phosphate, can compete with inorganic phosphate and replace the phosphate in the glycolytic and cellular respiration pathways [14,18].

It has been reported that long-term animal bioassays of MMA(V) with doses higher than the maximum threshold level of 400 ppm in the feed did not induce any tumors [16]. However, DMA(V) was found to be a bladder carcinogen only in rats and only when administered in the diet or drinking water at high doses [16]. The red blood cells of different animal species have different rates of uptake, reduction and methylation of DMA(V). In most animal species, DMA(V) does not usually enter the cells and is excreted unchanged. In a human study, approximately 70% of a single oral dose of DMA(V) was found to be excreted in urine as unchanged DMA(V) within 4 days [16].

Arsenic and human disease: an overview

Non-carcinogenic health effects

Symptoms of acute As toxicity include severe projectile vomiting and watery diarrhea, muscular cramp, facial edema as well as cardiac abnormalities [20].

Chronic effects of As exposure in humans have been well-reviewed and summarized by several research groups [14,18,21–25]. Human health effects caused by As have been found to be dependent on the magnitude of As exposure [14,24], source of As exposure [24], host factors [7,13–15,17–19] as well as the exposure duration [24] and exposure route [20]. Many different body systems are affected by chronic exposure to As. However, the most affected organs are those involved in As absorption, accumulation and excretion [22], including the gastrointestinal, cardiovascular, urinary, hepatic, dermal systems [22]. Some of these systems and the signs of chronic effects are summarized in Table 1 [14,18–20,22–24]. Of the symptoms caused by chronic effects, dermal lesions are the most abundant, and have also been known to occur within a period of about five years [23]. However, the shortest exposure period that has been reported for the manifestation of As toxicity is about 8 months [20].

Table 1 Non-carcinogenic human health effects observed after chronic As exposure

Organ system	Effects
Gastrointestinal	Portal hypertension, gastrointestinal hemorrhage
Cardiovascular	Peripheral vascular disorder- black foot disease, high blood pressure
Urinary	Proximal tubule degeneration, papillary and cortical necrosis
Hepatic	Hepatomegaly, portal fibrosis, cirrhosis, altered heme metabolism
Dermal	Skin lesions (hyperpigmentation, hyperkeratosis, desquamation, loss of hair)
Nervous	Peripheral neuropathy, encephalopathy
Hematological	Bone marrow depression (anemia, leucopenia, thrombocytopenia)
Endocrine	Diabetes, hormone regulation and hormone mediated gene transcription suppression
Respiratory and pulmonary	Cough, bronchitis, chest sound, shortness of breath
Reproduction	Fetal loss, necrosis, apoptosis, conception in the uterus, death of newborn, premature delivery, decreased birth weight of infants

From References 14, 18–20, 22–24.

The skin is known to localize and store As because of its high keratin content, which contains several sulfydryl groups to which As(III) may bind [23]. Moreover, verbal IQ and long-term memory can also be affected due to chronic As toxicity [24]. A strong relationship between chronic ingestion of As and deleterious human health effects has been observed [24]. Chronic effects of As exposure have been reported at various As concentrations ranging from $< 10\ \mu g \cdot L^{-1}$ to several thousand $\mu g \cdot L^{-1}$. Therefore, the US EPA has set the oral reference dose (RfD) of As at $3.0 \times 10^{-4} mg \cdot kg^{-1}$ (body-weight)$\cdot day^{-1}$ as the threshold value for non-carcinogenic effects of As [22]. Theoretically, the RfD is an estimate of a daily oral exposure to the human population, including the sensitive population that is likely to be without an appreciable risk of deleterious effects during a lifetime. Thus, the non-carcinogenic effects of As are expected to be observed in individuals who ingest more than the RfD of As on a daily basis.

Carcinogenic health effects

Inorganic As is classified by the International Agency for Research on Cancer [4,26] and the Integrated Risk Information System of the US EPA [22] as a known human carcinogen. This classification is based on several epidemiological studies, which have shown a positive association between exposure to As and development of cancer in many countries [18,24]. There is epidemiological evidence for lung, bladder, liver, kidney, colon, prostate and skin cancers being caused by exposure to As [14,20–23,25,27]. A strong association between As exposure and risk of several internal cancers can be observed when As levels in drinking water are very high ($> 150\ \mu g \cdot L^{-1}$) [28]. Exposure to arsenic even at a level of $50\ \mu g \cdot L^{-1}$ could easily result in a combined cancer risk in the order of 1 in 100 [29]. The lifetime risk of dying from cancer from daily ingestion of 1 L of water containing $50\ \mu g \cdot L^{-1}$ of As could be as high as 13 per 1000 people exposed [25]. Khan *et al*. [20] found that arsenical cancers systematically appeared first on the skin followed by internal organs [20]. It is believed that the mechanisms by which these cancers originate may involve the promotion of oxidative stress by As compounds, in which the antioxidant capacity of the living organism is overwhelmed by reactive oxygen species (ROS), resulting in molecular damage to proteins, lipids and, most significantly, DNA [14].

Arsenic occurrence in groundwater in Southeast Asia

Vietnam

Since the mid-1990s, the groundwater resources in the large alluvial deltas of the Red River in northern Vietnam, as well as the Mekong River in southern Vietnam, have been exploited for domestic use by private tube-wells [30]. High levels of As have been detected in the groundwater of the Red River delta and was first reported in 2001 (Table 2) [31], but the contamination of groundwater with As in the Mekong River delta was first reported in 2005 (Table 2) [32]. The Mekong River delta in Vietnam covers an area of 39 713 km^2. Since 2007, comprehensive studies of As groundwater contamination have been conducted in the Mekong River delta region. A broad groundwater survey was first conducted from May to November 2007 in 4 provinces located in the Mekong River delta, including An Giang, Dong Thap, Kien Giang and Long An. Core samples were subsequently collected from An Giang and Dong Thap Provinces in May 2008. Rice grain, drinking water and human hair samples were finally collected from two districts (An Phu and Phu Tan) in An Giang Province in November 2009.

The results of groundwater analyses revealed that most elemental concentrations other than those of As, Fe and Mn in groundwater samples collected from 4 provinces in the Mekong River delta during the rainy season were well below the WHO drinking water guidelines. Approximately half of the groundwater samples collected from An Giang and Dong Thap contained As concentrations higher than the WHO and national guideline level of $10\ \mu g \cdot L^{-1}$ (Fig. 3). However, no sample from Kien Giang or Long An was found to exceed the

Table 2 Geodemographic data of naturally occurring As in groundwater in Southeast Asia

Country	Population at risk	Level of As ($\mu g \cdot L^{-1}$)	Year of first discovery	National standard of As in drinking water ($\mu g \cdot L^{-1}$)	References
Vietnam				10	
- Red River delta	10 000 000	1–3 100	2001		3, 5, 31
- Mekong River delta	1 000 000	ND–1 351	2005		32, 33
Cambodia	100 000	Up to 3 500	1999	50	41
Lao PDR	Unknown	ND–278	2001	50	2, 3, 5
Thailand	15 000	1.3–5 114	1988	50	65, 66

Fig. 3 A map of arsenic groundwater contamination in Southeast Asia.

As guideline. The As concentrations in An Giang groundwater were found to be positively correlated with the total organic carbon (TOC) and Ba concentrations, but negatively correlated with the well depth, pH, and Mn, Ca, Mg, Na, Co, Ni and Si concentrations. However, positive correlations were found between the As, TOC and Ba concentrations in the groundwater of Dong Thap. Negative correlations were also found between the As level and distance from the well to the Mekong River, pH and Si concentration in the groundwater collected from the Dong Thap Province. The spatial influence on the groundwater As concentration manifested in the co-variation of the As concentration with depth and distance of the well from the Mekong River. In the An Giang Province, sampling sites within 2 km from the Mekong River had mean As concentrations nearly 10-fold higher than those at distances beyond 2 km ($P < 0.01$). The observed variation in As concentration in groundwater with distance from the Mekong River suggested that the Mekong River plays an important role in contamination of the local aquifer. Depending on the intensity of interactions between river water and groundwater, more or less contamination may be expected [33]. Shallow wells usually exhibited higher As concentrations, whereas deep wells appeared to be unaffected [33]. No spatial influence on the As concentration was found for groundwater in Kien Giang and Long An Provinces [33].

The highest concentrations of As in core samples collected from An Giang and Dong Thap provinces were found at depths of 46 and from 34.5 to 34.9 m, respectively. Relatively high As concentrations were detected in the brown and black-to-brown clay layers with approximate pH values of 7.5, while the concentrations of As in yellow-to-brown clammy clay, and brown-to-gray and fine-to-medium grain sand were lower than $5\ mg \cdot kg^{-1}$. Moreover, the concentrations of As and Fe in core samples were found to vary considerably depending on the depth. In general, the levels of As and Fe in core samples were relatively high in subsurface zones, but gradually decreased with depth. A strong correlation was found between the total As and Fe concentrations in the core samples (Pearson's $r = 0.4$; $P < 0.05$). As in sediments was mainly in the poorly crystalline iron oxide phase (37%–85%), which may explain the strong correlation observed between the total As and Fe concentrations. Only very few core samples contained As associated with the surface adsorbed phase or the manganese oxide phases. The organic matter and exchangeable phases contained small amounts of As. The reason for the positive correlation between the As and Fe concentrations in core samples but not in the groundwater samples may be that after being dissolved and released from aquifer sediments to groundwater, As and Fe may be affected by other processes, causing their concentrations to vary independent of each other [33]. The total As concentration in core samples was found to be strongly correlated with the As level in the poorly crystalline Fe oxide phase (Pearson's $r =$

0.95; $P < 0.01$). The high proportion of As found in Fe oxide-related phases in core samples provided convincing evidence that such phases were the principal source of As released to groundwater. However, the reductive dissolutions of the Fe and Mn phases were not necessarily dominant sources of As release to groundwater. Local hydro-biogeochemical conditions in the aquifer (including the presence of sedimentary organic matter or other electron donors, indigenous microorganisms, groundwater oxidation-reduction potential (ORP), pH, and the combined effects of coexisting ions in groundwater) may control the leaching of As from sediments to groundwater [33].

While contamination of groundwater with As in the Mekong River delta of Vietnam has been well-addressed, information about As and other elements in rice is not readily available.

The concentration of As in the polished rice grain samples (n = 39) collected from the target areas (An Phu and Phu Tan districts, An Giang Province) ranged from 132 to 471 $\mu g \cdot kg^{-1}$, with a mean value of 224 $\mu g \cdot kg^{-1}$ [35]. This result was in good agreement with the range of 96 to 465 $\mu g \cdot kg^{-1}$ (mean value of 215 $\mu g \cdot kg^{-1}$) of polished rice (n = 30) from the northern region of Vietnam reported by Tran *et al*. [34].

The amount of daily inorganic As intake through drinking water and rice consumption for all households in the Mekong River delta region was estimated based on the assumption that 100% and 80% of the total As was inorganic As contained in groundwater and rice grains, respectively. According to this assumption, groundwater contributed the most to the daily As intake, while rice may only contribute negligible amounts. However, rice can sometimes account for as much as 99% of the daily inorganic As intake in households that have water filter columns and access to safe water [35]. Unfortunately, water filtration systems were not common in the study area. Vietnamese residents usually cook rice with only the necessary amount of water that gets absorbed during the cooking process, so that no excess water is discarded. Thus, all of the As in the rice grains is preserved and readily enters the human body [36,37]. However, since the local people typically use the same water source for drinking and cooking, the actual As intake from rice may be higher [38]. Dermal absorption of As may be a significant route of exposure, particularly in those residents using As-contaminated groundwater for daily life activities, such as washing, cleaning and bathing.

It has been established that As levels in hair typically range from 0.02 to 0.2 $\mu g \cdot g^{-1}$ for individuals without As exposure and from 3 to 10 $\mu g \cdot g^{-1}$ in persons exposed to groundwater containing increased levels of As [39]. In the study of As concentration in human hair in An Giang Province, about 67% (n = 44), 42% (n = 28) and 15% (n = 10) of hair samples from the target area contained As levels exceeding 1, 3 and 10 $\mu g \cdot g^{-1}$, respectively. The highest As concentration (37.7 $\mu g \cdot g^{-1}$) was observed in a hair sample obtained from an 18-year-old female from the Phu Vinh, Cho Vam village in the Phu Tan district of An Giang Province [35]. Interestingly, the hair sample of the subject's 42-year-old mother also contained a high level of As (15.8 $\mu g \cdot g^{-1}$) and the hair sample of the subject's 41-year-old father contained the highest As level (8.9 $\mu g \cdot g^{-1}$) among the 22 male participants. This family had been consuming groundwater containing 336 $\mu g \cdot L^{-1}$ of As until 2008, when they transitioned to As-free tap water. The concentration of As in the rice consumed by the subjects was determined to be 225 $\mu g \cdot kg^{-1}$. As concentration in human hair from individuals living in the study location was significantly higher than that of individuals in the control area (P = 0.011). A paired sample t-test did not reveal any significant differences between the mean As levels in female and male hair samples (P = 0.103), although female hair samples displayed a wider range and higher average concentration of As than the male hair samples. Positive correlations between daily inorganic As intake and total As concentrations in female and male hair samples were significant. Excessive levels of As were observed in the hair of residents even one year after they had last consumed As-contaminated groundwater. The arsenic concentration in human hair may reduce as daily As intake decreases. However, the minimum time required to observe any change in the As levels of hair has not yet been defined. Monitoring As levels in hair after a period of exposure can improve our understanding of As detoxification. This field survey did not uncover any case of As poisoning or even a symptom of skin lesion at an early stage. Therefore, the possibility of arsenicosis symptoms in the local community is still an issue of concern.

Cambodia

In Cambodia, unsafe concentrations of As in shallow groundwater were first documented by the Japanese International Cooperation Agency (JICA) in its initial unpublished draft report, named "The study on groundwater development in Southern Cambodia," submitted to the Cambodia Ministry of Rural Development in 1999 [40]. Concurrently, the Ministry of Rural Development also conducted a national drinking water quality assessment in 13 provinces of Cambodia with support from WHO. The assessment indicated that 3 wells in Kandal Province had elevated concentrations of As [41]. In response to this discovery, As field test kits were used to test tube wells in a number of provinces to verify the magnitude of As hazards at groundwater access points. Additionally, the Royal Government of Cambodia established the Arsenic Inter-Ministerial Subcommittee in 2001 to formulate a government policy. An interim Cambodia standard for As concentration in drinking water of 50 $\mu g \cdot L^{-1}$ was adopted in 2003 as its first action (Table 2) [41]. Subsequently, numerous studies have documented As biogeochemistry and its health impacts in Cambodia. Several investigations [30,42–47] have described the distribution of

As concentrations in Cambodian shallow groundwater. The chemical, biological and physical processes that control heterogeneous As distribution in groundwater have also been widely studied [30,42–44,48–53]. Dangerous As concentrations have been observed in areas along the Mekong River (Fig. 3), particularly in Kratie, Prey Veng and Kandal Provinces, where As(III) was predominantly found in the reducing groundwater [40,46,48,51]. However, As(V) has mainly been observed in the oxidizing groundwater in Kampong Cham Province [40]. There has been a general agreement that the reductive dissolution of As-rich Fe (oxy) hydroxides may drive the release of As to groundwater [52]. This mechanism was also observed to be true in the Mekong River basin, Cambodia [48,51]. Using hydrologic and biogeochemical measurements, Polizzotto *et al*. [52] showed that As was released from the near-surface, river-derived sediments within the Mekong River delta and transported back to the river by groundwater flow through the underlying aquifer on a centennial time scale.

Although many populations live alongside watersheds in Cambodia, shallow groundwater is still the main source of drinking water [40]. This dependence on shallow groundwater is due to the lack of safe water supplies and water treatment systems in rural areas and the long dry season (November to May), which causes poor rainwater catchment. Additionally, a cutting edge campaign of water and sanitation that took place in the early 1990s promoted groundwater as microbiologically-clean and safe to use without any treatments. Consequently, many families were able to secure supposedly safe water through inexpensive and easily-drilled borehole tapping into the shallow aquifer groundwater [40]. Arsenic treatment systems, modified from traditional sand filters, have also been developed to enhance As removal from groundwater following the discovery of spatial and temporal variations in the groundwater composition [55]. However, no systematic and comprehensive field applications of As removal technologies have been performed in Cambodia due to concerns associated with their operations, efficacies and maintenance requirements [41]. The development of visual arsenicosis symptoms has generally been assumed to follow a decade of consumption of As-rich groundwater. However, new cases discovered in Cambodia have followed exposure times as short as 3 years, due to the extremely elevated As concentration in groundwater (3 500 $\mu g \cdot L^{-1}$), socioeconomic status, malnutrition, individual health status and hygiene, as well as drinking water maintenance and storage habits [40,41]. In fact, Mazumder *et al*. [56] found 70 cases ($n = 97$) in Preak Russey village of Kandal Province that showed evidence of arsenical skin lesions with either pigmentation or keratosis, and clinical and laboratory tests confirmed the lesions according to WHO's diagnostic criteria. The largest number of cases was seen within the 31–45 years old group, and both genders were more or less equally affected. Evidence of both pigmentation and keratosis were found in 60 cases, while only pigmentation and only keratosis was observed in 6 and 4 cases, respectively. In addition, Mazumder *et al*. [56] revealed that 37.0% of children in the less than 16 years old group had skin lesions of arsenicosis. The youngest child with evidence of keratosis and pigmentation was 8 years old, although the features of redness and mild thickening of the palms were observed even in children aged 4–5 years old.

A recent cross-sectional health risk assessment of inorganic As intake among Cambodian residents living in the Mekong River basin through the groundwater drinking pathway using the US EPA model revealed that thousands of Cambodians were at high risk of both toxic and carcinogenic effects of As. Approximately, 98.7% and 13.5% of the residents of the Kandal and Kratie Provinces, respectively, were at risk of As toxicity. Moreover, the cancer risk index indicated an average of 5 in 1 000 exposure in the Kandal Province study area [40].

The cancer risk index indicated in the study was the cancer risk caused specifically by As. The carcinogenic effects of As can be estimated as the incremental probability of an individual developing cancer over a lifetime as a result of exposure to a potential carcinogen. The cancer risk (CR) levels can be assessed as $CR = 1 - \exp(-CDI \times SF)$, where CDI is a chronic daily intake of As ($mg \cdot kg^{-1} \cdot d^{-1}$), SF is an oral cancer slope factor of As ($1.5\ mg \cdot kg^{-1} \cdot d^{-1}$) [57]. In general, the US EPA considers the cancer risks that are below about 1 chance in 1 000 000 (1×10^{-6}) to be so small as to be negligible and those of about 1×10^{-4} to be sufficiently large that some kind of remediation is desirable. Therefore, cancer risks ranging between 1×10^{-6} and 1×10^{-4} are generally considered to be acceptable [58].

Although significant regional differences in both toxic effects and cancer risks of As were observed, there were no significant differences in gender and age groups. Therefore, the health risk from As poisoning was more dependent on groundwater As concentrations, the average daily dose and other factors related to groundwater consumption, such as exposure duration and ingestion rate, rather than an individual's status, such as gender or age [40]. The latest stage of As skin cancer was also reported in the Mekong River basin of Cambodia. Cutaneous lesion characteristic of chronic arsenicosis had manifested and squamous cell carcinomas requiring amputation had developed in the individual [59].

To detect the early warning stage of chronic arsenicosis, an appropriate biomarker of arsenic exposure should be promptly validated. A biomarker (biological marker) is defined as a substance, physiologic characteristic, or genetic status that indicates or may indicate the present of disease, a physiologic abnormality or a physiologic condition [60]. A positive correlation between groundwater As concentration and As concentration in scalp hair was observed in the Mekong River basin of Cambodia [40,54,61,62]. In addition, Gault *et al*. [61] assessed the use of total As concentration in nail and hair as a biomarker of arsenic exposure from drinking As-rich groundwater, while Kubota *et al*. [54] utilized hair As

and urinary 8-hydroxy-2′-deoxyguanosine (8-OHdG) to verify As toxicity. Recently, Phan *et al*. [63] validated the use of As concentration in scalp hair, fingernails and toenails as biomarkers by studying exposure-biomarker relationships. It was found that As concentrations in scalp hair, fingernails and toenails were positively associated with groundwater As concentration and an individual's average daily dose of arsenic, suggesting that As concentrations in scalp hair, fingernails and toenails can be used as biomarkers of chronic arsenic exposure from drinking As-rich groundwater. Of the three biomarkers, As concentration in scalp hair is more favorable due to the ease of sample processing and measurement. Interestingly, the study suggested that the three biomarkers reflected different time windows of exposure. As concentration in scalp hair might reflect past exposure of 2–5 months prior to hair cutting; As concentration in fingernails was more likely to indicate past exposure of 6–12 months, while that in toenails might depict past exposure as long as 12–18 months before clipping [63]. Since arsenicosis continues to be a major public health concern in rural Cambodia, the application of biomarkers may prove useful in detecting early stages of chronic As exposure and thus avoiding further harm. The onset of arsenicosis symptoms are generally assumed to manifest following a decade of suspected exposure to As. Nonetheless, simpler diagnostic tools to detect and monitor chronic arsenicosis should be encouraged, as testing for biomarkers is not always feasible in rural areas such as those in Cambodia [63]. Furthermore, Sampson *et al*. [41] have suggested that management of groundwater in Cambodia with high levels of As would be possible through identification of risk areas, comprehensive educational programs, and enforcement of the policy formulated by the Royal Government of Cambodia, to facilitate the development of alternative water supplies and educational programs.

Lao People's Democratic Republic

Unlike other areas such as the Mekong valley in Cambodia and Vietnam, where problems with groundwater As contamination have been well documented, little data are so far available in areas of Lao PDR. In 2001, the UNICEF carried out preliminary testing of groundwater from wells in several areas of Lao PDR, including Attapeu, Savannakhet, Champasak, Saravane, Sekong, Khammuane and Bolikhamxai. Analysis of 200 samples indicated that some samples had As concentrations greater than 10 $\mu g \cdot L^{-1}$. Only one well in the Attapeu Province was found to contain water with an As level (112 $\mu g \cdot L^{-1}$) exceeding the national standard for As in drinking water of 50 $\mu g \cdot L^{-1}$ [64]. Even though the current maximum permissible concentration for As in drinking water recommended by WHO is 10 $\mu g \cdot L^{-1}$, Lao PDR still uses the former WHO-recommended concentration of 50 $\mu g \cdot L^{-1}$ as the national standard for As in drinking water due to economic considerations and lack of tools and techniques to measure lower As concentrations accurately [3]. In 2004, the UNICEF, in collaboration with the government of Lao PDR and the Adventist Development and Relief Agency, tested approximately 680 tube-well water samples taken from the Holocene aquifer in the Mekong valley areas, and reported that 21% of all samples had As concentrations exceeding the WHO guideline for drinking water (10 $\mu g \cdot L^{-1}$) while 1% exceeded the national standard (50 $\mu g \cdot L^{-1}$) [3].

During 2007 and 2008, Chanpiwat *et al*. [2] investigated the enrichment of As and As speciation in groundwater collected from either household or community tube wells located along the Mekong River in Lao PDR (Vientiane, Bolikhamxai, Savannakhet, Saravane, Champasak, and Attapeu). It was found that about 55.7% of all 61 samples had As concentrations exceeding the WHO guideline for drinking water (10 $\mu g \cdot L^{-1}$). The highest As concentration (278 $\mu g \cdot L^{-1}$) was found in the Champasak Province. The percentages of tube well samples in each province containing As levels higher than the WHO guideline were 20% for Attapeu, 28.6% for Bolikhamxai, 76.9% for Champasak, 54.6% for Saravane and 100% for Savannakhet (Fig. 3). Moreover, approximately 14.8% of all samples contained As concentration higher than the national standard for As (50 $\mu g \cdot L^{-1}$) in drinking water. Tube-well water samples containing As levels higher than 10 $\mu g \cdot L^{-1}$ were collected mostly from the middle and southern parts of the country. The areas along the Mekong River below the middle part are generally floodplains and are occupied by Quaternary sediments transported by the Mekong River. In addition, the results of this recent study [2] clearly showed that tube-well water samples with pH less than 6.5 and low redox potential generally had high As concentrations ($> 10 \mu g \cdot L^{-1}$). Therefore, an acidic pH and reducing conditions were concluded to be the major environmental factors enhancing the release of As from sediments. High As concentrations, such as those found in this study along the Mekong River in the central and southern Lao provinces, may thus have arisen under the reducing (anaerobic) conditions created in young (Quaternary) alluvial and deltaic aquifers.

The As concentrations in tube wells in Lao PDR (ND–277.8 $\mu g \cdot L^{-1}$) were relatively lower than those found in the areas along the Mekong River of Cambodia and Vietnam (Table 2). The Mekong valleys of Cambodia and Vietnam have lower topographic gradients than that of Laos. Consequently, both areas may contain larger amounts of young alluvial soils. In addition, the As found in Champasak, Saravane and Attapeu may also be contributed in part by ancient volcanic activities that occurred millions of years ago [2]. In metamorphic environments, As principally presents as arsenopyrite (sulfide minerals) precipitated from hydrothermal fluids [1]. Fengthong *et al*. [64] also concluded based on their studies of surface and groundwater contamination and drinking water quality in Lao PDR that the threat of naturally occurring As in groundwater was associated with certain geological formations.

In term of As speciation, 45.9% of all 61 tube-well samples had total As concentrations dominated by As(III) [2]. Compared to As(V), another As inorganic species, As(III) is fairly soluble in water and generally regarded as being more acutely toxic than As(V) [7]. After entering the human body, As(III) is readily absorbed from the GI tract into the bloodstream and then distributed widely among the internal organs [7]. As has also been proposed to cause chromosomal abnormalities that lead to cancer, particularly skin cancer, and cancer of internal organs, such as lung, bladder, and kidney [7]. As(III) was the dominant As species in the tube-well water samples obtained from Bolikhamxai, Champasak, Saravane and Savannakhet. Concentrations of As(III) in the tube-well water samples varied from $< 0.05\ \mu g \cdot L^{-1}$ (in Bolikhamxai, Champasak, and Saravane) to $274.95\ \mu g \cdot L^{-1}$ (in Champasak), with an average concentration of $18.72\ \mu g \cdot L^{-1}$ [2]. However, the tube-well water collected from Attapeu and Vientiane had mainly As(V) and particulate As, respectively [2].

According to Chanpiwat *et al*. [2], the observed concentrations of total As as well as different As species clearly revealed that villagers living in the middle and southern regions of Lao PDR, especially in the Bolikhamxai, Savannakhet, Saravane and Champasak Provinces, have been subjected to detrimental health effects due to the consumption of As-enriched groundwater. However, the health effects of As exposure and estimations of area and population at risk should be further examined to ascertain the scale of the threat posed by As contamination.

Thailand

In Thailand, As has never been reported to naturally occur [65]. Groundwater As contamination in this country has been reported to originate from both point sources (leachate from ore dressing plant wastes) and diffuse sources (underground placer deposits) [65,66]. An area well-known to be affected by As is the Ron Phibun District, Nakhon Si Thammarat Province, on the southern peninsula of Thailand (Fig. 3). The Ron Phibun District lies within the Southeast (Main Range) Tin Belt of southern Thailand with respect to geology, metallogenesis and mining history [67]. The primary Sn-W-As mineralization and alluvial placer tin deposits were mined here for over 100 years [68]. However, the mining sites were closed by the Department of Mineral Resources in 1990 [69]. As a result of the mining operations, high-grade arsenopyrite, pyrite-rich waste piles, and waste from ore dressing plants and panning were generated. High rainfall aided in the leaching out of toxic minerals such as As, leading to contamination of soil, groundwater and surface water with As over an area of $500\ km^2$ within the district [67,69,70]. Health problems linked to As in drinking water were first highlighted in the residents of the Ron Phibun District in 1987 due to a case of arsenical skin cancer in a female resident [67,68,71]. In 1988, a preliminary survey on the extent, distribution and epidemiology of arsenicosis in the province was established by the Ministry of Public Health. It was reported that approximately 1 000 cases were diagnosed with As-induced skin disorders, including keratosis and melanosis. In 1994, a collaborative study between the Thai and the British government authorities on the geochemical form of As in aquifer systems in the affected area revealed that As contamination of shallow ground water ranged between 1.25 and $5\ 114\ \mu g \cdot L^{-1}$ (Table 2). About 69.6% of the 23 shallow wells contained As concentrations exceeding the WHO guideline for drinking water ($10\ \mu g \cdot L^{-1}$). Moreover, 39.1% of all collected samples had As levels above the national groundwater quality standard of $50\ \mu g \cdot L^{-1}$ [67]. Furthermore, it was found that piped water in this area had an As concentration of $70\ \mu g \cdot L^{-1}$ [72]. At the time the problems were first recognized, about 15 000 villagers were estimated to be drinking water with more than $50\ \mu g \cdot L^{-1}$As [68] (Table 2).

Arsenic speciation data showed high absolute As(III) concentrations ($> 50\ \mu g \cdot L^{-1}$) in several of the shallow groundwater samples, although As(V) remained the dominant species throughout (As(III) = 2.4% to 6.1% of total As) [67]. More recently, As concentrations in both shallow groundwater and shallow well pumps have been reported to exceed the WHO guideline for drinking water ($> 700\ \mu g \cdot L^{-1}$ and $10\ \mu g \cdot L^{-1}$, respectively) [69]. However, Tseng [71] concluded that wells deeper than 60 feet from the level of limestone and slate were safe from As contamination.

Since the Chao Phraya River valley contains relatively young sediments that could develop a combination of geochemical conditions, such as reducing or oxidizing conditions and high pH, that allow the release of As, this area may also suffer from contamination of groundwater with As. A survey of groundwater As concentration was recently conducted in the groundwater sources located near a river in central Thailand [65]. A total of 37 samples were collected from shallow aquifers around a lower Chao Phraya River basin area of Nakhonpathom Province. Arsenic concentrations in most of the shallow wells were about $5\ \mu g \cdot L^{-1}$ or less, with an average of $11\ \mu g \cdot L^{-1}$. Based on these results, Kohnhorst [65] concluded that As contamination of groundwater was not of public health significance in Central Thailand. In addition, most households have easy access to high-quality treated water making the possibility of arsenicosis very low in this region [65].

Role of the Mekong River in arsenic groundwater contamination

Countries in SEA generally have several common hydrological features, which have been recognized as the main causes of naturally occurring As in groundwater, including: 1) alluvial and low-lying flat topographies, 2) rapid Holocene sedimentation nourished by large rivers, 3) an abundance

of degradable organic material, and 4) slow-moving groundwater [1,5]. The Mekong delta is one of the floodplains well-known for As-enriched groundwater in the region [73]. Groundwater As problems along the Mekong valley, which covers parts of Lao PDR, Cambodia and Vietnam, have been reported by numerous studies [2,5,30,32,33,40,46,47,73]. The delta plain of the Mekong River delta spans a 62 520 km^2 area in Vietnam (about 83%) and Cambodia [74]. This river delta is likely to play a significant role as an efficient trap for collecting alluvial materials moved by the Mekong River system due to Quaternary relative sea level changes [74,75]. The decomposition of organic matter-rich sediments can enhance the reducing (low redox potential) conditions in the aquifer sediments [3,6,8]. As a result, As mobilization can occur at acidic pH via the reductive dissolution of iron oxides. Metal oxides (particularly iron oxides) and sulfide minerals (particularly pyrite) are the most important mineral sources in aquifers [3]. Since a large amount of As is adsorbed onto iron oxides, once iron reducing conditions are established in the aquifer, As can be either desorbed from the surface of the dissolving Fe oxide or released from the mineral structure itself [3,44,76]. However, to initiate this process, a source of degradable organic carbon, such as those available in the alluvial sediments, as well as microbial activities, are essential [3,76]. So far few investigations have been carried out in the Mekong valley as a whole. Most investigation to date appears to have been carried out in Cambodia and Vietnam. It was found that high Fe and Mn concentrations and anaerobic conditions are common features of the groundwaters throughout the lowland areas of Cambodia. Areas of the great perceived risk with As concentrations greater than 50 $\mu g \cdot L^{-1}$ are those with Holocene sediments forming the main aquifer [5]. While As concentrations were found to be mostly low for groundwaters from Holocence deposits [5]. Different As concentrations for those groundwaters were found in the Middle and Upper Pleistocene deposits ($<$ 1–32 $\mu g \cdot L^{-1}$), Lower Pleistocene deposits ($<$ 1–7 $\mu g \cdot L^{-1}$), Pliocene deposits ($<$ 1–57 $\mu g \cdot L^{-1}$) [5].

Arsenic mitigation measures in Southeast Asia

As reported by the World Bank [3], the operational responses to As groundwater contamination in most SEA countries have undertaken so far. Interestingly, Non-Governmental Organizations (NGOs) and international organizations seem to have been the main drivers, rather than government organizations. Indeed no country has taken major steps towards active and strategic monitoring of Asian groundwater [3].

In response to As contamination of groundwater in SEA, several approaches have been implemented to mitigate the levels of As in groundwater to an acceptable level ($<$ 10 $\mu g \cdot L^{-1}$). Several membrane filtration units, supported by the United Nations University, GIST, and WoongJin Chemicals in South Korea, were installed in the Champasak Province of Lao PDR and the An Giang Province of Vietnam in December and May 2010, respectively. The installation of more filtration units are being processed in the Dong Thap Province of Vietnam by Can Tho University in collaboration with GIST.

After the discovery of As contamination of groundwater in Cambodia in 1999 by JICA, the Royal Government of Cambodia formed an interior subcommittee to regulate As concentration in drinking water, with a permissible limit of arsenic set at 50 $\mu g \cdot L^{-1}$, which is as low as it is in other developing countries. Testing of wells was conducted in a number of provinces to identify the arsenic-affected areas using arsenic field test kits. Concurrently, several NGOs developed information, education and communication (IEC) materials to educate the affected communities about the risks of consuming arsenic-rich groundwater. Similarly, an educational program for school children was developed and implemented in a few schools in high-risk areas. Wells found to have arsenic concentrations higher than the Cambodian national standard were painted red to indicate that the water is not safe for drinking, as is the practice in Bangladesh. This kind of educational effort was partly successful in some communities [41]. However, the positive impact of this initiative was significantly reduced due to successive installation of large numbers of new tube wells in areas at high risk of arsenic contamination without proper arsenic testing. Arsenic removal units have recently been installed by the Institute of Technology of Cambodia (ITC) in several affected communities in the Kandal and the Prey Veng Provinces, with technical and financial support from Lehigh University in the USA. Each of those units was expected to provide arsenic-safe water for approximately 200 households. However, an educational program is needed to mobilize people to collect arsenic-safe water from the units.

Concluding remarks

Our review of published work revealed that the knowledge of the occurrence and distribution of As has improved greatly over the last few years. As contamination of groundwater in the SEA region is a serious problem, especially in the floodplain areas along the Mekong River. Arsenic generally occurs and is enriched in aquifers through the reductive dissolution of river-derived sediments containing iron oxides. Young sediments in alluvial and deltaic plains are obvious target areas for further investigation. Groundwater containing As concentration greater than the WHO guideline for drinking water ($>$ 10 $\mu g \cdot L^{-1}$) is consumed by local people on a daily basis, especially in the form of drinking water. Due to the carcinogenic nature of As, visual arsenicosis, such as arsenical skin lesions with pigmentation or keratosis, can develop and can be observed in residents continuously exposed to As-contaminated groundwater, even for exposure

times shorter than 10 years. However, there are still knowledge gaps regarding As especially on the epidemiological side. The scope of public health concern on As contamination in medium and long terms is not yet clear. To ascertain the scale of the threat of As a systematic assessment of risk areas, As epidemiology, social and cultural conditions, as well as patient identification and treatment should be conducted. Appropriate technical solutions for As mitigation that are practical to the local conditions in terms of technology, cost-benefit ratio and social considerations should be developed. Moreover, raising awareness through educational programs as well as direct action and enforcement by governments should be immediately taken for sustainable As mitigation.

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References

1. Schmoll O, Howard G, Chilton J, Chorus I. Protecting groundwater for health: Managing the quality of drinking-water resources. World Health Organization. London: IWA publishing, 2006
2. Chanpiwat P, Sthiannopkao S, Cho KH, Kim KW, San V, Suvanthong B, Vongthavady C. Contamination by arsenic and other trace elements of tube-well water along the Mekong River in Lao PDR. Environ Pollut 2011; 159(2): 567–576
3. The World Bank, the Water Sanitation Program. World Bank policy report: towards a more effective operational response. Arsenic contamination of groundwater in South and East Asian Countries. Massachusetts:The International Bank for Reconstruction and Development, 2005
4. International Agency for Research on Cancer (IARC). IARC monographs on the evaluation of carcinogenic risks to humans, Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42. http://monographs.iarc.fr/ENG/Monographs/suppl17-19.pdf (Access on June 26, 2011)
5. Rahman MM, Naidu R, Bhattacharya P. Arsenic contamination in groundwater in the Southeast Asia region. Environ Geochem Health 2009; 31(Suppl 1): 9–21
6. Smedley PL, Kinniburgh DG. A review of the source, behavior and distribution of arsenic in natural waters. Appl Geochem 2002; 17(5): 517–568
7. Adriano DC. Trace elements in terrestrial environments: biogeochemistry, bioavailability, and risk of metal. 2nd ed. Springer-Verlag, NY, USA, 2001
8. Islam FS, Gault AG, Boothman C, Polya DA, Charnock JM, Chatterjee D, Lloyd JR. Role of metal-reducing bacteria in arsenic release from Bengal delta sediments. Nature 2004; 430(6995): 68–71
9. Stüben D, Berner Z, Chandrasekharam D, Karmakar J. Arsenic enrichment in groundwater of West Bengal, India: geochemical evidence for mobilization of As under reducing conditions. Appl Geochem 2003; 18(9): 1417–1434
10. Rowland HAL, Polya DA, Lloyd JR, Pancost RD. Characterisation of organic matter in a shallow, reducing, arsenic-rich aquifer, West Bengal. Org Geochem 2006; 37(9): 1101–1114
11. Anawar HM, Akai J, Komaki K, Terao H, Yoshioka T, Ishizuka T, Safiullah S, Kato K. Geochemical occurrence of arsenic in groundwater of Bangladesh L sources and mobilization processes. J Geochem Explor 2003; 77(2–3): 109–131
12. Routh J, Hjelmquist O. Distribution of arsenic and its mobility in shallow aquifer sediments from Ambikanagar, West Bengal, India. Appl Geochem 2011; 26(4): 505–515
13. Thomas DJ. Arsenolysis and thiol-dependent arsenate reduction. Toxicol Sci 2010; 117(2): 249–252
14. Jomova K, Jenisova Z, Feszterova M, Baros S, Liska J, Hudecova D, Rhodes CJ, Valko M. Arsenic: toxicity, oxidative stress and human disease. J Appl Toxicol 2011; 31(2): 95–107
15. Abernathy CO, Thomas DJ, Calderon RL. Health effects and risk assessment of arsenic. J Nutr 2003; 133(5 Suppl 1): 1536S–1538S
16. Cohen SM, Arnold LL, Eldan M, Lewis AS, Beck BD. Methylated arsenicals: the implications of metabolism and carcinogenicity studies in rodents to human risk assessment. Crit Rev Toxicol 2006; 36(2): 99–133
17. Roy P, Saha A. Metabolism and toxicity of arsenic: a human carcinogen. Curr Sci 2002; 82(1): 38–45
18. Hughes MF. Arsenic toxicity and potential mechanisms of action. Toxicol Lett 2002; 133(1): 1–16
19. Masotti A, Sacco LD, Bottazzo GF, Sturchio E. Risk assessment of inorganic arsenic pollution on human health. Environ Pollut 2009; 157(6): 1771–1772
20. Khan MM, Sakauchi F, Sonoda T, Washio M, Mori M. Magnitude of arsenic toxicity in tube-well drinking water in Bangladesh and its adverse effects on human health including cancer: evidence from a review of the literature. Asian Pac J Cancer Prev 2003; 4(1): 7–14
21. Khan MA, Ho YS. Arsenic in drinking water: a review on toxicological effects, mechanism of accumulation and remediation. Asian Journal of Chemistry 2011; 23(5): 1899–1901
22. Integrated Risk Information System (IRIS). http://www.epa.gov/IRIS/ (Access on July 27, 2011)
23. Duker AA, Carranza EJM, Hale M. Arsenic geochemistry and health. Environ Int 2005; 31(5): 631–641
24. Kapaj S, Peterson H, Liber K, Bhattacharya P. Human health effects from chronic arsenic poisoning—a review. J Environ Sci Health A Tox Hazard Subst Environ Eng 2006; 41(10): 2399–2428
25. Rahman MM, Ng JC, Naidu R. Chronic exposure of arsenic via drinking water and its adverse health impacts on humans. Environ Geochem Health 2009; 31(Suppl 1): 189–200
26. International Agency for Research on Cancer (IARC). Arsenic in drinking water 1. Exposure data — IARC monographs. http://monographs.iarc.fr/ENG/Monographs/vol84/mono84-6A.pdf (Access on August 18, 2011)
27. Benbrahim-Tallaa L, Waalkes MP. Inorganic arsenic and human prostate cancer. Environ Health Perspect 2008; 116(2): 158–164
28. Cantor KP, Lubin JH. Arsenic, internal cancers, and issues in inference from studies of low-level exposures in human populations. Toxicol Appl Pharmacol 2007; 222(3): 252–257

29. Bonior DE. Public exposure to arsenic in drinking water in Michigan. http://oversight-archive.waxman.house.gov/documents/20040607132512-45841.pdf (Access on August 19, 2011)
30. Berg M, Stengel C, Trang P P, Hungviet M, Sampson M, Leng S, Samreth D, Fredericks. Magnitude of arsenic pollution in the Mekong and Red River Deltas—Cambodia and Vietnam. Sci Total Environ 2007; 372(2–3): 413–425
31. Berg M, Tran HC, Nguyen TC, Pham HV, Schertenleib R, Giger W. Arsenic contamination of groundwater and drinking water in Vietnam: a human health threat. Environ Sci Technol 2001; 35 (13): 2621–2626
32. Stanger G, Truong TV, Ngoc KS, Luyen TV, Thanh TT. Arsenic in groundwaters of the lower Mekong. Environ Geochem Health 2005; 27(4): 341–357
33. Hoang TH, Bang S, Kim KW, Nguyen MH, Dang DM. Arsenic in groundwater and sediment in the Mekong River delta, Vietnam. Environ Pollut 2010; 158(8): 2648–2658
34. Phuong TD, Kokot S, Chuong PV, Tong Khiem D. Elemental content of Vietnamese rice. Part 1: sampling, analysis, and comparison with previous studies. Analyst (Lond) 1999; 124(4): 553–560
35. Hoang TH, Bang S, Kim KW, Nguyen MH. Community exposure to arsenic in the Mekong River delta, southern Vietnam. J Environ Monit 2011; 13: 2025–2032
36. Sengupta MK, Hossain MA, Mukherjee A, Ahamed S, Das B, Nayak B, Pal A, Chakraborti D. Arsenic burden of cooked rice: traditional and modern methods. Food Chem Toxicol 2006; 44(11): 1823–1829
37. Signes A, Mitra K, Burló F, Carbonell-Barrachina AA. Contribution of water and cooked rice to an estimation of the dietary intake of inorganic arsenic in a rural village of West Bengal, India. Food Addit Contam Part A Chem Anal Control Expo Risk Assess 2008; 25(1): 41–50
38. Ohno K, Yanase T, Matsuo Y, Kimura T, Hamidur Rahman M, Magara Y, Matsui Y. Arsenic intake via water and food by a population living in an arsenic-affected area of Bangladesh. Sci Total Environ 2007; 381(1–3): 68–76
39. Cleland B, Tsuchiya A, Kalman DA, Dills R, Burbacher TM, White JW, Faustman EM, Mariën K. Arsenic exposure within the Korean community (United States) based on dietary behavior and arsenic levels in hair, urine, air, and water. Environ Health Perspect 2009; 117(4): 632–638
40. Phan K, Sthiannopkao S, Kim KW, Wong MH, Sao V, Hashim JH, Mohamed Yasin MS, Aljunid SM. Health risk assessment of inorganic arsenic intake of Cambodia residents through groundwater drinking pathway. Water Res 2010; 44(19): 5777–5788
41. Sampson ML, Bostick B, Chiew H, Hangan JM, Shantz A. Arsenicosis in Cambodia: case studies and policy response. Appl Geochem 2008; 23(11): 2976–2985
42. Polya DA, Lythgoe PR, Abou-Shakra F, Gault AG, Brydie JR, Webster JG, Brown KL, Nimfopoulos MK, Michailidis KM. IC-ICP-MS and IC-ICP-HEX-MS determination of arsenic speciation in surface and groundwaters: preservation and analytical issues. Mineral Mag 2003; 67(2): 247–261
43. Polya DA, Gault AG, Diebe N, Feldman P, Rosenboom JW, Gilligan E, Fredericks D, Milton AH, Sampson M, Rowland HAL, Lythgoe PR, Jones JC, Middleton C, Cooke DA. Arsenic hazard in shallow Cambodian groundwaters. Mineral Mag 2005; 69(5): 807–823
44. Buschmann J, Berg M, Stengel C, Winkel L, Sampson ML, Trang PT, Viet PH. Contamination of drinking water resources in the Mekong delta floodplains: arsenic and other trace metals pose serious health risks to population. Environ Int 2008; 34(6): 756–764
45. Quicksall AN, Bostick BC, Sampson ML. Linking organic matter deposition and iron mineral transformations to groundwater arsenic levels in the Mekong delta, Cambodia. Appl Geochem 2008; 23(11): 3088–3098
46. Sthiannopkao S, Kim KW, Sotham S, Choup S. Arsenic and manganese in tube well waters of Prey Veng and Kandal Provinces, Cambodia. Appl Geochem 2008; 23(5): 1086–1093
47. Luu TT, Sthiannopkao S, Kim KW. Arsenic and other trace elements contamination in groundwater and a risk assessment study for the residents in the Kandal Province of Cambodia. Environ Int 2009; 35(3): 455–460
48. Rowland HAL, Gault AG, Lythgoe P, Polya DA. Geochemistry of aquifer sediments and arsenic-rich groundwaters from Kandal Province, Cambodia. Appl Geochem 2008; 23(11): 3029–3046
49. Lear G, Song B, Gault AG, Polya DA, Lloyd JR. Molecular analysis of arsenate-reducing bacteria within Cambodian sediments following amendment with acetate. Appl Environ Microbiol 2007; 73(4): 1041–1048
50. Benner SG, Polizzotto ML, Kocar BD, Ganguly S, Phan K, Ouch K, Sampson M, Fendorf S. Groundwater flow in an arsenic-contaminated aquifer, Mekong Delta, Cambodia. Appl Geochem 2008; 23(11): 3072–3087
51. Kocar BD, Polizzotto ML, Benner SG, Ying SC, Ung M, Ouch K, Samreth S, Suy B, Phan K, Sampson M. Integrated biogeochemical and hydrologic processes driving arsenic release from shallow sediments to groundwaters of the Mekong delta. Appl Geochem 2008; 23(11): 3059–3071
52. Polizzotto ML, Kocar BD, Benner SG, Sampson M, Fendorf S. Near-surface wetland sediments as a source of arsenic release to ground water in Asia. Nature 2008; 454(7203): 505–508
53. Robinson DA, Lebron I, Kocar B, Phan K, Sampson M, Crook N. Time-lapse geophysical imaging of soil moisture dynamics in tropical deltaic soils: As aid to interpreting hydrological and geochemical processes. Water Resour Res 2009; 45:W00D342.
54. Kubota R, Kunito T, Agusa T, Fujihara J, Monirith I, Iwata H, Subramanian A, Seang Tana T, Tanabe S. Urinary 8-hydroxy-2′-deoxyguanosine in inhabitants chronically exposed to arsenic in groundwater in Cambodia. J Environ Monit 2006; 8(2): 293–299
55. Chiew H, Sampson ML, Huch S, Ken S, Bostick BC. Effect of groundwater iron and phosphate on the efficacy of arsenic removal by iron-amended BioSand filters. Environ Sci Technol 2009; 43(16): 6295–6300
56. Mazumder DN, Majumdar KK, Santra SC, Kol H, Vicheth C. Occurrence of arsenicosis in a rural village of Cambodia. J Environ Sci Health A Tox Hazard Subst Environ Eng 2009; 44(5): 480–487
57. Office of Emergency and Remedial Response, U.S. Environmental Protection Agency. Risk Interim final, EPA/540/1–89/002, 1989
58. Environmental Protection Agency. HH: Risk characterization. http://www.epa.gov/region8/r8risk/hh_risk.html (Access on July 27, 2011)
59. James GG, Adam CG, Colinda H, Erin MK, Kayla J, Say BV.

Arsenic and amputations in Cambodia. Asian Biomed 2010; 4(3): 469–474

60. Youngson RM. Collis dictionary of medicine. 4th ed. London: Harper Collins, 2007
61. Gault AG, Rowland HAL, Charnock JM, Wogelius RA, Gomez-Morilla I, Vong S, Leng M, Samreth S, Sampson ML, Polya DA. Arsenic in hair and nails of individuals exposed to arsenic-rich groundwaters in Kandal Province, Cambodia. Sci Total Environ 2008; 393(1): 168–176
62. Sthiannopkao S, Kim KW, Cho KH, Wantala K, Sotham S, Sokuntheara C, Kim JH. Arsenic levels in human hair, Kandal Province, Cambodia: the influences of groundwater arsenic, consumption period, age and gender. Appl Geochem 2010; 25(1): 81–90
63. Phan K, Sthiannopkao S, Kim KW. Surveillance on chronic arsenic exposure in the Mekong River basin of Cambodia using different biomarkers. Int J Hyg Environ Health 2011 Aug 4. [Epub ahead of print]
64. Fengthong T, Dethoudom S, Keosavanh O. Drinking water quality in the Lao People's Democratic Republic. Seminar on the environmental and public health risks due to contamination of soils, crops, surface and groundwater from urban, industrial, and natural sources in South East Asia, Hanoi, Vietnam. December 2002, UN-ESCAP
65. Kohnhorst R, Kunito T, Agusa T, Fujihara J, Monirith I, Iwata H. Arsenic in groundwater in selected countries in South and Southeast Asia: a review. J Trop Med Parasitol 2005; 28: 73–82
66. Caussy D. Epidemiological methods for mitigating health impacts of arsenic in South East Asia region of the World Health Organization. http://www.b*vs*de.ops-oms.org/b*vs*acd/arsenico/Arsenic2004/theme1/paper1.2.pdf
67. Williams M, Fordyee F, Paijitprapapon A, Charoenchaisri P. Arsenic contamination in surface drainage and groundwater in part of the Southeast Asian tin belt, Nakhon Si Thammarat Province, southern Thailand. Environmental Geology 1996; 27(1): 16–33
68. Smedley PL. Sources and distribution of arsenic in groundwater and aquifers. In: Appelo T. Arsenic in groundwater — a world problem. Proceedings of seminar Utrecht 29 November 2006. http://www.iah.org/downloads/occupub/arsenic_gw.pdf
69. Jindal R, Ratanamalaya P. Investigations on the status of arsenic contamination in southern Thailand. In: International Water Association (IWA). Southeast Asian Water Environment 1. London: IWA Publishing, 2006: 223–229
70. Ruangwises S, Saipan P. Dietary intake of total and inorganic arsenic by adults in arsenic-contaminated area of Ron Phibun district, Thailand. Bull Environ Contam Toxicol 2010; 84(3): 274–277
71. Tseng CH. Chronic arsenic intoxication in Asia: current perspectives. www.tsim.org.tw/journal/jour10-6/P10_224.PDF
72. Kadushkin A, Siddiqui Z, Shipin O. Groundwater quality assessment and management in selected countries of East and Southeast Asia. 2004. http://www.b*vs*de.paho.org/b*vs*acd/cd63/groundwater-quality.pdf
73. The World Bank, the Water Sanitation Program. World Bank policy report: volume II technical report. Arsenic contamination of groundwater in South and East Asian Countries. Massachusetts: the International Bank for Reconstruction and Development, 2005
74. .Lap Nguyen V, Oanh TK, Tateishi M. Late Holocene depositional environments and coastal evolution of the Mekong River Delta, Southern Vietnam. J Southeast Asian Earth Sci 2000; 18(4): 427–439
75. Lu XX, Siew RY. Water discharge and sediment flux changes in the Lower Mekong River. Hydrol Earth Syst Discuss 2005; 2(6): 2287–2325
76. Winkel L, Berg M, Stengel C, Rosenberg T. Hydrogeological survey assessing arsenic and other groundwater contaminants in the lowlands of Sumatra, Indonesia. Appl Geochem 2008; 23(11): 3019–3028