Abstract

Arsenic occurs naturally in the earth’s crust and is widely distributed in the environment. Natural mineralization and activities of microorganisms enhance arsenic mobilization in the environment but human intervention has exacerbated arsenic contamination. Although arsenic is useful for industrial, agricultural, medicinal and other purposes, it exerts a toxic effect in a variety of organisms, including humans. Arsenic exposure may not only affect and disable organs of the body, especially the skin, but may also interfere with the proper functioning of the immune system. This paper, therefore, generally highlights the toxic effects of arsenic as well as its mobilization in the natural environment and possible controls. It also briefly attempts to outline the impact of arsenic on the immune system, whose alteration could lead to viral/bacterial infections.

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Keywords: Arsenic; Immune system; Anthropogenic; Microorganisms; Season

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1. Introduction

Arsenic occurs naturally as an element, ranks as the 20th most occurring trace element in the earth’s crust (NRC, 1977) and is widely distributed in the environment. Its association with some nonweathering-resistant mineral deposits (e.g., sulphide minerals) has contributed to its release in large amounts into the environment (Murdoch and Clair, 1986).

Arsenic exists mainly in three valency states (i.e., −3, +3, +5). The trivalent arsenic (As³⁺) and the pentavalent arsenic (As⁵⁺) are widely present in natural waters (Feng et al., 2001) and are soluble over a wide range of pH and Eh conditions (Bell, 1998). In oxidizing environmental conditions, As⁵⁺ species are more stable and predominant, whereas in reducing environmental conditions, As³⁺ species are predominant. Under anaerobic conditions, arsenite can be reduced to arsine by microorganisms in soil (Bachofen et al., 1995; Gao and Burau, 1997; Cheng and Focht, 1979).

Arsenic species may be methylated as monomethylarsonic acid (MMAA), dimethylarsinic acid (DMAA) and trimethylarsine oxide (TMAO) by microorganisms (Ridley et al., 1977; Woolson, 1977; Cullen and Reimer, 1989; Gadd, 1993), humans and animals. The trivalent compounds are generally more toxic than the pentavalent compounds (Smedley et al., 1996; Cervantes et al., 1994). The most toxic of them all is arsine gas (AsH₃; Buchet and Lauwers, 1983; Leonard, 1991). Organic arsenical compounds exist generally nontoxic (Gochfeld, 1995).

Arsenic is used in hardening of alloys and in production of semiconductors, pigments, glass manufacturing, pesticides, rodenticides and fungicides (Hatheway et al., 1991). It is also used as an ingredient of drugs for the treatment of some diseases (e.g., sleeping sickness, chronic myeloid leukemia; Nevens et al., 1990; Luh et al., 1973). Because of its usefulness and exploitation, arsenic contamination is now widespread in the environment. Inasmuch as toxic compounds of arsenic could occur naturally or anthropogenically in the environment, an understanding of its toxic effects is warranted.

In this paper, we present a review of pertinent literatures to highlight the general toxic effect of arsenic and specifically on the immune response, which when down-regulated can lead to opportunistic infections that are very often not considered as consequence of arsenic toxicity. We discuss further environments where, when and how arsenic may be enriched naturally or anthropogenically. Finally, we discuss some measures for treatment of arsenic poisoning.

2. Kinetics and metabolism of arsenic

Ingested elemental arsenic is considered less toxic, poorly absorbed and largely eliminated unchanged from the human body. However, soluble arsenic compounds are absorbed from the gastrointestinal tract (Hindmarsh and McCurdy, 1986) and eliminated (e.g., As⁵⁺, organic arsenic) via the kidney (Buchet et al., 1981; Luten et al., 1982; Tam et al., 1982). Trivalent arsenic (As³⁺) is removed from the body through urinary excretion of nonmethylated and methylated arsenic (As⁵⁺ and As³⁺). Methylated arsenic species are inorganic form of As³⁺ and As⁵⁺ sequentially reduced in vivo (Vahter and Envall, 1983; Winski and Carter, 1995), which are detoxified in the liver to MMAA and DMAA species. Both in vivo and in vitro studies show that these ‘detoxified’ species (MMAA and DMAA) are both toxic to humans and animals (Ochi et al., 1996; Petrick et al., 2001, 2000; Styblo et al., 2000; Kaise et al., 1989).

The methylation of arsenic, which in the past was solely considered as a detoxification process, has changed. Studies (e.g., Apohshian et al., 2000) have shown that trivalent methylated arsenicals (i.e., MMAA and DMAA) have been detected in urine samples of individuals exposed to inorganic arsenic. Animal studies and in vitro studies in human cells have shown that these methylated compounds are more toxic than the corresponding inorganic (i.e., As³⁺) (Yamanaka et al., 1991; Yamanaka and Okada, 1994; Styblo et al., 2000; Del Razo et al., 2001). This suggests that methylation may not only be a detoxification process but may also enhance toxicity and/or carcinogenesis. Farmer and Johnson (1990) report that about 40–60% of arsenic may be retained in the body even after exposure cessation and that this may be accumulated in the skin, hair, nails, muscle and small amounts in teeth and bones (ATSDR, 1990; Ishinishi et al., 1986).

3. Arsenic toxicity

Arsenic (e.g., As³⁺) can be toxic through its interaction with sulphhydril groups of proteins and enzymes (to denature the proteins and enzymes within the cells; Gebel, 2000; Graeme and Pollack, 1998) and through an increase of reactive oxygen species in the cells, consequently causing cell damage (Ahmad et al., 2000; Wang et al., 1996; Chen et al., 1998; Nies, 1999). Arsenic can interfere with essential enzymatic functions and transcriptional events in cells, leading ultimately to “multitude of multisystemic noncancer effects that might ensue” (NRC, 1995). For example, oxidative stress induced by trivalent methylated arsenicals inhibits glutathione (GSH) reductase (Styblo et al., 1997) and thioredoxin reductase (Lin et al., 1999) with subsequent impairment of cellular protective mechanism against oxidants. While depletion of cellular GSH sensitizes cells to arsenicals and may also contribute to cell transformation (Shimizu et al., 1998), thioredoxin depletion affects gene expression due to the fact that it modulates DNA binding activity of some transcriptional factors (Matthews et al., 1992; Arrigo, 1999; Powis et al., 2000). Arsenite is known to inhibit more than 200 enzymes in the body (Abernathy et al., 1999) and, because arsenate has a similar structure as phosphate, it can substitute for phosphorus in the body,
which can lead to replacement of phosphorus in the bone for many years (Arena and Drew, 1986; Ellenhorn and Barceloux, 1988). Because arsenate is hydrolyzed easily (in the cell), it prevents subsequent transfer of phosphate to adenosine diphosphate (ADP) to form adenosine triphosphate (ATP; the energy currency of the cell) and thus depletes the cell of its energy (Winship, 1984). Arsine, the most toxic of the arsenicals (Buchet and Lauwerys, 1983; Leonard, 1991), is known to cause hemolysis of red blood cells, leading to hemolytic anaemia, which is primarily responsible for the development of oliguria renal failure (Fowler and Weissberg, 1974; Fowler, 1977). It has been suggested that arsenic interacts with sulfhydryl group of proteins and enzymes (Levinsky et al., 1970) may be responsible for inhibition of erythrocyte sodium-potassium pump. It also is known that arsenic decreases DNA repair process (Brochmoller et al., 2000) and, hence, enhances susceptibility to cancer (e.g., skin cancer; Wei et al., 1994) and noncancer-related diseases (Feng et al., 2001).

4. Chronic effects of arsenic

Arsenic toxicity could affect a wide variety of organisms, including humans (Cervantes et al., 1994). Chronic arsenic effects in humans have been well documented and reviewed (e.g., Webb, 1966; Klevay, 1976; Pershagen, 1983). Organs most affected are those involved with arsenic in absorption, accumulation and/or excretion. These organs are the gastrointestinal tract, circulatory system, liver, kidney, skin, tissues very sensitive to arsenic and those tissues secondarily affected (e.g., heart; Squibb and Fowler, 1983). Signs of chronic arsenic toxicity include dermal lesions (e.g., hyperpigmentation, hyperkeratosis, desquamation and loss of hair; Zaloga et al., 1985), peripheral neuropathy, skin cancer and peripheral vascular disease. These signs have been observed mostly in populations whose drinking water contains arsenic (Tseng, 1977; Tseng et al., 1968; Zaldivar, 1980; Zaldivar and Ghai, 1980; Cebrian et al., 1983; Smith et al., 2000). Among these symptoms, dermal lesions were most dominant, and were also known to occur within a period of about five years. The skin is known to localize and store arsenic because of its high keratin content, which contains several sulfhydryl groups to which As3+ may bind (Kitchin, 2001) and may be the reason for its sensitivity to arsenic toxic effect. A study of Tseng (1977) in the Province of Taiwan (China) established a clear dose-response relationship between arsenic and dermal lesions, Blackfoot disease (BFD; a peripheral vascular disorder) and skin cancer. From several studies (e.g., Chen and Wu, 1962; Chi and Blackwell, 1968; Tseng, 1977; Chen et al., 1988a,b; Engel et al., 1994), it has been established that peripheral vascular diseases are associated with arsenic in well water in Taiwan. However, vascular disease has also been reported among German vintners (Grobe, 1976), inhabitants of Antofagasta and Chile (Borgono et al., 1977). Skin cancers, including in situ cell carcinoma (or Bowen’s disease), invasive cell carcinoma and multiple basal cell carcinomas, are all known to be associated with chronic arsenic exposure (Shneidman and Belizaire, 1986; Tseng et al., 1968; Yeh et al., 1968; ATSDR, 1990). Chen et al. (1995) observed that hypertension was linked to long-term arsenic ingestion as well as cerebrovascular disease (i.e., cerebral infection). Other effects are hematopoietic depression, anhydremia (due to loss of fluid from blood into tissue and the gastrointestinal tract), liver damage characterized by jaundice, portal cirrhosis and ascites, sensory disturbance and peripheral neuritis, anorexia and loss of weight (Webb, 1966).

Although the effects of arsenic, as recounted above, result in several kinds of diseases, it certainly may also impact adversely on the immune system, which may predispose to viral/bacterial infections. Several of such diseases resulting from alterations of the immunologic surveillance may not have been known to be due to arsenic and therefore may not have been attributed to arsenic effects. A probing into this area is therefore appropriate.

5. Immune system response

5.1. Animal studies

Aranyi et al. (1985) studied the immune effects of arsenic in animals and reported that inhalation of arsenic trioxide by mice caused an increased susceptibility to respiratory bacterial pathogens (i.e., Klebsella pneumonia) apparently via injury to alveolar macrophages. A report by Hatch et al. (1985) also indicated significant increases in mortality in mice, which were infected with bacterial pathogens after intratracheal injection of sodium arsenate. Gainer and Pry (1972) reported of inhibition of interferon action by arsenic in mice (as compared to controls) when mice were dosed with sodium arsenite prior to viral inoculation. Blakely et al. (1980) also found that levels of arsenite (0.5–10 ppm) in drinking water produced immune suppressive effects in mice, which demonstrated an inhibitory effect on the immune system. Studies (Dai et al., 1999; Lantz et al., 1994) have shown that arsenic is immunosuppressive and that it enhances susceptibility to infections (Vos, 1977; Gainer and Pry, 1972; Aranyi et al., 1985; Lantz et al., 1994). Furthermore, studies by Kaltreider et al. (2001) showed that arsenic disrupts the hormone glucocorticoids, which helps to regulate the immune system, central nervous system, and changes in blood, bone and kidneys as well as the body’s use of sugars, starches, fats and proteins.

5.2. Human studies

A study by Gonsebatt et al. (1994), using subjects whose drinking water contained mean arsenic concentration of 412 \( \mu g \, L^{-1} \) (i.e., arsenic-exposed) and controls whose drinking
water had mean arsenic concentration of 37 µg l⁻¹, found impairment in the immune response of the arsenic-exposed subjects. Samet et al. (1998) found that the transcriptional factors (c-Jun, ATF-2, substrate of JNK and p38) were markedly phosphorylated in BEAS cells when treated with As³⁺, with MAPKs inducing interleukin-8 (IL-8) protein expression. They speculated that such activation were likely to result in cellular responses, such as growth proliferation, apoptosis and modulated inflammatory expression. Harrison and McCoy (2001) suggested that apoptosis might be an important mechanism for arsenic-induced immunosuppression. However, when apoptosis malfunctions, it leads to several kinds of diseases, including cancer (Miller and Marx, 1998). Furthermore, Frenkel et al. (2002) report that arsenic impairs the immune system.

A study by Rosales-Castillo et al. (2004) in the Lagunera Region of Mexico assessed the relationship between chronic arsenic exposure, human papilloma virus (HPV), contact and nonmelanoma skin cancer (NMSC) and concluded that viral infection (i.e., HPV) could constitute an additional risk factor for the development of NMSC among populations chronically exposed to arsenic. Other researchers (Grimmel et al., 1988; Gerdsen et al., 2000) had previously found HPV in arsenic-induced lesions, such as squamous cell carcinoma and keratoses. The above findings may be viewed from the background that arsenic may cause a defect in cell-mediated immune function, compromise its protective mechanism and thus enhance viral intervention.

Arsenic also causes anemia (ATSDR, 2000; Parish et al., 1979), the severity of which indicates the extent of disruption to normal regulatory mechanisms exerted by the macrophages and the T-cells (Sathe et al., 1990; Bogner et al., 1990; Gascon et al., 1993); and also acts as an antagonist to selenium (Se), affecting its metabolism in vivo (Miyazaki et al., 2003; Schrauzer, 1987). In Taiwan, Lin and Yang (1988) studied Blackfoot disease (BFD) patients; a disease associated with arsenic (Tseng, 1977, 1989; Tseng et al., 1968, 1995, 1996; Chen et al., 1988b; Chi and Blackwell, 1968) and reported lower concentrations of Se and Zn in urine and blood of BFD patients than controls. The deficiency of micronutrients (e.g., Se, Zn) is associated with malnutrition (Houssaini et al., 1997) and may also alter the immune function (Good et al., 1980). Zinc, for example, is essential for normal immune function (Good et al., 1980; Vruwink et al., 1993; McMurray et al., 1990; McMurray and Yetley, 1983). Selenium also occurs in the enzyme Glutathione peroxidase in human erythrocytes (Auasthi et al., 1975). It is suggested that the enzyme Glutathione peroxidase together with vitamin E protect cell membrane against oxidative damage (Gibson and Scythes, 1984). Selenium therefore may act to negate the toxic effect of arsenic, which not only induces oxidative stress (Miyazaki et al., 2003) but also is capable of down-regulating inflammatory cytokines (e.g., Th-1; Frenkel et al., 2002; Vega et al., 1999; Gainer and Pry, 1972). Guanqing (1979) suggested that Keshan disease which is prevalent in some areas of China and associated with selenium deficiency (Chen et al., 1980; Xu et al., 1985) could be a viral disease exacerbated by selenium deficiency or low selenium and low proteins. The deficiency of these micronutrients may therefore predispose to immunoincompetence (Golden et al., 1978) and could lead to susceptibility to opportunistic pathogens to establish infection (Cunningham-Rundles and Lin, 1998).

6. Arsenic and microorganisms

Certain microbes can adapt to arsenic toxicity (Cervantes et al., 1994; Silver et al., 1993) and a wide range of microorganism can thrive in toxic arsenic-enriched environments (Ahmann et al., 1994; Macrae and Edwards, 1972; Laverman et al., 1995). In order for these microorganisms to thrive and function in this (arsenic) environment, several have developed resistance to arsenic toxicity (Nakahara et al., 1977). The resistance is due to reduced uptake of arsenate and increased concentrations of phosphate transport into bacterial cells (Harold and Baarda, 1966; Bennett and Malamy, 1970; Willsky and Malamy, 1980). This phenomenon of decreased arsenate and increased phosphate uptake results from intracellular competition between arsenate and phosphate (Thiel, 1988). In addition to being resistant to arsenic toxicity, certain microorganisms are able to reduce the less toxic arsenate form to the more toxic arsenite (Andreae, 1978, 1979; Ji and Silver, 1995; Nies and Silver, 1995; Rensing et al., 1999). The reduction is an energy-generating process for the microorganism (Ilyaeledtinov and Abridshitova, 1981); however, the impact of such arsenic geochemistry in anoxic systems cannot be underestimated, especially with respect to arsenic mobilization (Ahmann et al., 1997; Cummings et al., 1999).

7. Arsenic-enriched environments

Although microorganisms play an essential role in the environmental fate of arsenic in relation to mechanisms of arsenic transformations (e.g., soluble and insoluble forms, toxic and nontoxic forms; Nealson, 1997; Lovley, 1997; Banfield et al., 1998), human activities have exacerbated arsenic contamination in the environment (Bell, 1998). Examples of human activities that have adversely affected the environment are mining, waste disposal, indiscriminate use of fertilizers, pesticides, herbicides, manufacturing and chemical spillage. In 1979, for example, the total amount of arsenic released into the environment (in the United States) as a result of anthropogenic activities was estimated to be 5.3 x 10⁶ kg (U. S. EPA, 1982), of which 81% was deposited on land. Jahan et al. (2002) report that in the state of Victoria (Australia), mining of gold had caused an estimated 30,000 tonnes of arsenic to be redistributed to the surface across the
landscape through erosion into streams and rivers. Many incidents of arsenic contamination of the environment have been reported in several countries of the world. The situation can have significant adverse influence on health due to arsenic uptake in water and food especially by developing and rural populations who depend on local sources of food and water. Therefore, any arsenic geochemical anomaly may impact negatively on health (Plant et al., 1996). Some examples of arsenic-enriched environments are described below.

7.1. Agricultural environments

Although the dominant source of arsenic in soils is the parent rock (Smedley and Kinniburgh, 2002), pesticides and phosphates can substantially enhance arsenic concentration in soils. Arsenic has been used and is still used as pesticides, insecticides and in cattle and sheep dips (Azcue and Nriagu, 1989). In soils, Arsenic has been measured and is still used as pesticides, insecticides, and in cattle and sheep dips (Azcue and Nriagu, 1994), for control of moth in fruit crops (Buchanan, 1977; Yoon and Kim, 1977). Between the 1920s and the 1980s, several sheep and cattle dips (to control tick) were built by the State Government of Australia. The dips numbering 1647 were situated every couple of miles and stretched from tropical Queensland to New South Wales. The soil around the dips was contaminated with arsenic. Arsenic levels measured in some of the disposal pits were up to about 3000 ppm (Lloyd-Smith and Wickens, 2000). Arsenicate portrays certain characteristics of phosphates through its absorption by ligand exchange on hydrous iron and aluminium oxide (Davies and Jones, 1988). Hence, arsenic accumulates in soil, contaminates both surface and groundwater (Lloyd-Smith and Wickens, 2000), is taken up by plants and is then entrenched in mammalian/insectivore food chain (Green et al., 2001). Irrigation, especially with wastewaters, can cause a problem of build-up of mobile and potentially toxic metals (e.g., arsenic) in soils and in surface runoff (Siegel, 2002).

7.2. Mining-related environments

Mining activities cause arsenic to be released in high concentrations from oxidized sulphide minerals (Smedley and Kinniburgh, 2002). This has resulted in high concentrations of arsenic in surface water (Smedley et al., 1996; Williams et al., 1996; Azcue et al., 1994), groundwater (Smedley and Kinniburgh, 2002; Del Razo et al., 1990; Armienta et al., 1997), soil and vegetation (Amasa, 1975).

7.3. Riverine and volcanic environments

Several studies (e.g., Nriagu, 1979, 1989; Nriagu and Pacyna, 1988 Lantz and Mackenzie, 1979) have shown that volcanoes are important natural sources of arsenic especially in the Southern Hemisphere (Nriagu, 1989; Nriagu and Pacyna, 1988). Under high temperatures (e.g., volcanic eruptions), arsenic is very mobile in the fluid phase and may also be present in fumaroles as sublimes and incrustations (Signorelli, 1993). Volcanic ashes are also known to contribute to or generate high arsenic concentration in waters (Smedley and Kinniburgh, 2002; Nicoll et al., 1989) probably by reason of their reactive nature, and due to the acidic material as well as the fine-grained volcanic ash, which could generate low pH in surface and groundwaters.

7.4. Lakes and reservoir environments

Arsenic concentrations in lakes compared to those in rivers or streams may be lower due to adsorption of arsenic in iron oxides in neutral conditions. Lakes and reservoir environments are, however, often impacted by geothermal activity, which can enhance arsenic concentrations (Aggett and Kriegman, 1988). Arsenic concentrations in lakes and reservoir environments can also increase due to low water flow (Smedley and Kinniburgh, 2002; Nimick et al., 1998) and to containment of water by natural and anthropogenic means. Construction of dams or reservoirs on rivers can, therefore, promote arsenic enrichment in the contained water. In Ghana, Armah et al. (1998) measured arsenic concentrations in contained water south of the Weija dam (an impoundment on the Densu River that stores water for the western part of the capital city, Accra). Levels of arsenic concentration from 100 m and 12 km downstream of the impoundment were 19.1 and 14.0 mg l⁻¹, respectively. Buruli ulcer (BU), a mycobacterial disease, is endemic and generally higher in settlements proximal to the impoundment.

7.5. Flooded environments

Flooding induces (anaerobic) reducing conditions in soils (Deuel and Swoboda, 1972; Hess and Blanchar, 1977; McGeehan and Naylor, 1994; Reynolds et al., 1999). Under this condition, As⁵⁺ is reduced to As³⁺ and adsorbed As⁵⁺ is released as As³⁺ (Reynolds et al., 1999; Massacheleyen et al., 1991; Rochette et al., 1998). Floods carry along sediments and/or contaminants that have been stored (for short periods, several decades or even a millenium) in river beds and other sediments preserved in local low-energy environments such as behind bedrock obstructions in valley floor or alcoves developed in valley walls. Floods and/or storm waters can therefore carry along metals that contaminate the environment (Miller, 1997). For example, alluvial soils in Thailand could contain up to 5000 mg g⁻¹ of arsenic (Thornton and Farago, 1997). Such contaminations through flooding increase and become severe with time and pose health hazard both to wildlife and humans (Bickford et al., 1999; Stoughton and Marcus, 2000).

7.6. Alluvial and deltaic environments

The most serious occurrences (involving large populations) of arsenic exposure in groundwater in alluvial and
deltaic environment with resultant health problems are in Bangladesh and West Bengal (India; BGS and DPHE, 2001; DPHE/BGS/MML, 1999; Smedley and Kinniburgh, 2002). Alluvial and deltaic environments are mostly characterized by reducing conditions, which cause high arsenic concentrations in groundwater (Smedley and Kinniburgh, 2002). In these environments, aquifer sediments do not allow air to enter (the aquifer) and coupled with the fact that recent sediments contain organic matter (which uses available oxygen), result in the development of reducing conditions (Smedley and Kinniburgh, 2002). Such conditions, which favour mobilization of arsenic, are also found in wetlands. Wetlands are effective filters for metal-containing water due to the high metal-binding affinity of their soils (Beining and Ote, 1996). In these environments, reducing conditions result in increased concentration of arsenic in solution, which are dominated by As$^{3+}$ species.

8. Seasonal variation

Seasonal variation affects, in general, metal concentration and particularly arsenic speciation both in water and soil, apparently due to biologic uptake (Andreae, 1978, 1979). Temperature changes, particularly during dry spells, may help to potentiate metal toxicity (Savage et al., 2000). Drop in water levels in certain parts of the tropical world during dry season expose arsenic-enriched substrate to air resulting in their oxidation. For arsenopyrite-rich rocks, aqueous oxidation of arsenic by dissolved oxygen is described by the following equation: $4\text{FeAsS} + 3\text{O}_2 + 6\text{H}_2\text{O} = 4\text{Fe}^{2+} + 4\text{AsO}_4^{3-} + 4\text{SO}_4^{2-} + 12\text{H}^+$. Under aerobic conditions, As$^{5+}$ species predominate. However, under most reducing conditions, As$^{3+}$ species predominate. Where pH decreases, much more arsine gas and dimethylarsine develop, which are released from surfaces of marshy soil or swamps and grass surfaces (Cheng and Focht, 1979). Based on several studies (Thornton and Farago, 1997; Andreae, 1978, 1979; Savage et al., 2000; Sohrin et al., 1997; Michel et al., 1999), the arsenic cycle could be described as follows: The dry period is a preparatory stage in which arsenic-rich beds (pyrites/arsenopyrites) are exposed to air and oxidized. Dissemination of oxidized arsenic into streams or rivers starts at the onset of the rainy season. The rainwaters during wet season solubilize oxidized arsenic or secondary minerals and disseminate them into the ecosystems through floods or storm waters (Rodriguez et al., 2004). The time, therefore, of observation of the toxic effect of arsenic will be after the recession of the floods (i.e., dry season) during which the cycle repeats. Interestingly, Sarkodie et al. (1997) found that the period in which crops contained the highest concentration of both arsenic species (As$^{3+}$ and As$^{5+}$; in an arsenic contaminated environment) to be in the months of September and October; the same period during which incidence for the onset of BU peaks in both Ghana and Côte d’Ivoire (Amofah et al., 1993; Marston et al., 1995). During the dry season, toxicity of arsenic (i.e., proportion of As$^{3+}$ to As$^{5+}$) may be enhanced by high temperatures and extreme evaporation (Maest et al., 1992). The increase in As$^{3+}$ and its mobility (McLaren and Kim, 1995) may be linked to the depletion of oxygen levels especially in the bottom of lakes due to microbial reduction (Azcue and Nriagu, 1995).

9. Treatment and control

A range of chelating agents has been used in arsenic poisoning. These include D-penicillamine, dimercaprol or British Antilewisite (BAL), Dimercaptosuccinic acid (DMSA), dimercaptopalanusulfonic acid (DMPS). These in general have been reported to be ineffective against arsenic poisoning (Hall, 2002). Others (Saha et al., 1999) report of the success of these agents but not when complications have developed. Wax and Thornton (2000) also reported of one case of success in the use of DMPS against peripheral neuropathy. The cost, however, of these chelating agents may not be affordable by most people (Saha et al., 1999). (Arsenic scourge seems to occur among rural populations of the developing world.) The best control measure may be to implement preventive rather than curative measures. This implies adhering to WHO minimum regulatory limit of 10 μg l$^{-1}$ of arsenic in water, improve water quality or find alternative water supply (e.g., rainwater harvesting) to the population to prevent altogether arsenic poisoning or morbidity. The above measures should be coupled with regular testing of wells (Hall, 2002) to detect any increase in arsenic concentration. Where farmlands are affected by arsenic contamination, soil remediation may be implemented.

10. Summary

- Arsenic occurs naturally as an element in the earth’s crust and is widely distributed in the environment. The trivalent species is more toxic than the pentavalent, but arsine gas is the most toxic of them all.
- Arsenic is promptly absorbed through the gastrointestinal tract and excreted in the urine as a mixture of As$^{3+}$, As$^{5+}$, MMMA and DMAA. Some arsenic may, however, remain bound to certain tissues.
- The toxicity of arsenic may be due to its reaction to sulfhydryl groups of proteins and enzymes, subsequently inhibiting the functioning of sensitive enzymes and leading ultimately to “multitude of multisystemic non-cancer effects that might ensue”.
- Organs most affected are the gastrointestinal tract, circulatory system, liver, kidney, nervous system, other sensitive tissues and the heart. The skin localizes and
stores arsenic because of its high keratin content and may be the reason for its high sensitivity to arsenic.

- Impairment of the immune system by arsenicals through chronic ingestion may involve susceptibility to opportunistic pathogens to establish infection.
- A wide range of microorganisms can thrive in toxic arsenic-enriched environments; having developed resistance mechanisms to function in that environment. The activities of these microorganisms enhance arsenic mobilization in the environment.
- There have been many incidents of arsenic contamination in the environment with resultant adverse health effects in several countries of the world. The causes of such contamination vary from agriculture and/or irrigation, geological changes, mining, natural intervention (such as floods) and groundwater exploitation.
- Seasonal variation also affects arsenic speciation both in water and soil, (often due to microbial intervention). Situation during such times, especially in dry periods, enhance arsenic toxicity.
- Chelating agents are known to be ineffective against arsenic poisoning especially in cases of malignancy.
- Adhering to WHO regulatory minimum limits, improving water quality or finding alternative water supply (e.g., rainwater) may be the best control measure against arsenic poisoning or morbidity.

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