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REVIEW PAPER

IMPACT OF LONG-TERM EXPOSURE TO ARSENIC ON CARDIOVASCULAR HEALTH – BRIEF NARRATIVE REVIEW

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Highlights

- Arsenic (As) plays a very important role on cardiovascular health.
- There is still a lack of accurate guidelines for rapid analysis of this element.
- Chronic and long-term exposure to As is a serious public health problem.

Abstract

Chronic and long-term exposure to heavy metals is a significant public health problem today. Development and globalization present challenges to constant control and monitoring, mainly of metals and toxic substances, including arsenic (As). It is estimated that nearly 200 million people worldwide are at serious risk of exposure. The purpose of this review is to summarize the impact of long-term of exposure to As on selected cardiovascular diseases in humans, based on the available literature. This narrative review provides an insight into the complexity of the processes of arsenic's influence on cardiovascular health and attempts to identify factors that may serve as potential preventive targets. Arsenic exposure has been associated with several cardiovascular outcomes, including hypertension, atherosclerosis, venous insufficiency, stroke, and myocardial infarction. Common exposure to As and other metals is inevitable, but it is worth noting that the difference in its toxicity may be due to gender, diet, exposure, and dose level, among other factors. Even in the case of the smallest and short-lived exposures, the poisonous and immensely damaging effects of As pose a serious risk of at least cardiovascular health, a major public health challenge as global growth continues. The challenge for future epidemiological and public health research on As and vascular diseases should be to study long-term exposure to As at the individual level in different groups. Reliable biomarkers with appropriate references to the sample should be used, individuals with low and moderate exposure should be included, and a modern genomic approach should be used to analyze genetic susceptibility. Med Pr Work Health Saf. 2025;76(6)

Key words: arsenic, arsenic speciation, public health, toxicity, cardiovascular health, chronically exposed

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INTRODUCTION

Arsenic (*Arsenicum* – As) is a naturally occurring element of the nitrogen group with metalloid properties and appears in 5 different valence states: +V (arsenate), +III (arsenite), +I (arsonium metal), 0 (arsenic), and –III (arsine). The As(III) (AsO_3^{3-}) is more toxic than As(V), because it more readily binds to sulfhydryl groups on proteins. The toxicity As(V) results from its reduction to As(III) in the human body [1–3]. Among approx. 20 known arsenic compounds, arsines include arsine (AsH_3), monomethylarsine ($(CH_3)AsH_2$), dimethylarsine ($(CH_3)_2AsH$), trimethylarsine ($(CH_3)_3As$), and diarsine (As_2H_4), with their respective boiling points [4]. Arsenic occurs mainly in the Earth's crust (2.5 ppm), including in groundwater, air, and land. It is highly toxic in its inorganic form (e.g. found in water), but less so in its organic form [1,2]. The literature on the subject most often indicates the range in terms of content and toxicity in the body, ranking 12th among other elements, and accumulates in the liver, kidneys, lungs, bones, and hair. The highest value refers to the content in the entire body. Low-level chronic exposure is defined as a daily intake of 0.002–0.02 mg As/kg acute exposure to high doses of approx. 2 mg/kg, and the toxic and lethal value is approx. even 13 mg/kg. The half-life of As is 7–10 h, and mostly accumulate in skin, nails and hair. Health problems caused by As can appear ≤40 years after exposure has ended [1,3–6]. This element formerly used as a traditional poison can be properly used, treating some types of cancer and often saving lives – in the latter case, when used in the right doses [3]. Chronic and long-term expo-

sure to heavy metals is a serious public health problem today. Development and globalization present challenges to constant control and monitoring, mainly of metals and toxic substances such as lead, cadmium, mercury, copper, or even As [1,4,7–10]. Worse still, exposure to ≥2 metals can result in cumulative negative consequences [2]. The International Agency for Research on Cancer has classified both As itself and its compounds among the most carcinogenic to humans, while the World Health Organization (WHO) has classified As as 1 of 10 toxic substances of major public health concern [1,11]. Almost 200 million people worldwide are at serious risk of exposure to As, raising serious concerns about their health and proper development [6,12]. Yet, in South Asia alone, this applies to >140 million people [13].

Until today, the focus has been on water or food contamination and the negative effects of As mainly on skin, lung, bladder cancers, developmental problems, and even diabetes [1,6,7,12]. It has been linked to adverse effects on pregnancy, kidney failure, or at least impaired behavioral problems (e.g., intelligence, impaired memory, psychosis) [1,2,5]. The available epidemiological data confirms some links between exposure to the element and cardiovascular health, although this has not been definitively established [2,7]. Undoubtedly, there is a constant search for new sources of information and biomarkers with high diagnostic utility in the course of cardiovascular diseases (CVDs), including the most common one – high blood pressure [14–16].

In humans, exposure to toxic As occurs through ingestion, inhalation, and skin contact [5]. Other important influences include dietary history, body mass index, lifestyle, age, gender, ethnicity, and inherited genetic traits, which can affect As methylation [4,17].

The most common characteristic effects of chronic As poisoning, even after a minimum of 5 years, manifest as skin changes (e.g., pigmentation changes, hard spots on hands and feet) or skin cancer. Acute poisoning (arsenicosis) includes vomiting, abdominal pain, burning stomach, garlic odor in the breath, and diarrhea. Extreme cases additionally include numbness and tingling of all limbs, muscle spasms, and even death [1,2,5]. In addition, cardiovascular symptoms may occur, including hypotension, heart failure, cardiac arrhythmia, cardiomyopathy, vascular disorders, and Raynaud's syndrome [5,6,11,18].

The purpose of this review is to summarize the impact of long-term exposure to As on selected CVDs in humans, based on the available literature. This narrative review provides an insight into the complexity of the processes of arsenic's influence on cardiovascular health and attempts to identify factors that may serve as potential preventive targets.

METHODS

The following manuscript offers a unique aspect, presenting the multidirectional impact of this element on public health, environmental impact and long-term exposure to As on cardiovascular health. This multidirectional combination provides a holistic view of the As toxicity problem. Selected articles formed the basis of this brief narrative review on topics related not only to the harmfulness of As itself but to its widespread availability in the environment, including drinking water. Due to the subject matter and its impact on health, elements of dietary and environmental sources, molecular aspects, and preventive measures were described. Attention was paid to the impact of this element on health, particularly on the cardiovascular system and its various subunits. The literature review refers the impact of long-term exposure to As and health effects in terms of selected CVDs. The search was limited to English-language articles and only in open access using the keywords: "hypertension," "atherosclerosis," "venous insufficiency," "stroke," "ischemic heart disease," "arsenic toxicity," and "arsenic speciation." Particular attention was given to the most recent research results available in the public literature, mainly from the last 15 years (January 2010 – May 2025) primarily from PubMed and Scopus. Earlier articles did not always refer to the indicated information, and there was often a lack of open access.

RESULTS

Effect of arsenic on cardiovascular diseases

While some studies have been devoted to individual carcinogens [19] and their impact on health, fewer have assessed their potential impact on CVD. Meanwhile, CVD is the most common cause of mortality and morbidity in Poland, Europe, and around the world [7,16,20]. In Poland alone, the number of deaths from this cause will peak in 2045, amounting to 223 300/year and accounting for >50% of estimated total deaths. The higher death rates still apply mostly to men. In Eastern Europe, 432.3/100 000 people died in 2022 [20,21]. Further, it is estimated that hypertension alone will account for >1.5 billion deaths worldwide in 2025 [11]. This data shows a clear difference in the incidence of CVD in the population by gender, and additional elim-

fecting endothelial dysfunction of the actin and smooth muscle [7,16,35,36]. Normal metabolism produces a wide range of ROS, which have several important physiological functions, such as being used by the immune system to kill pathogens, as well as rectify imbalances in the normal redox state caused by the accumulation of superoxides and free radicals (those with toxic effects, e.g., As), which damage all cell components (cellular components including proteins, lipids, and DNA). Accumulation of ROS can occur in the presence of inflammation and infection, and as a result of exposure to environmental factors, such as the adverse effects of As [4,37].

In the health effects of As longitudinal study in Bangladesh [30], an association has been shown between even low impact of exposure to As found in water and high impulsive pressure. Researchers additionally observed that the average intake of B vitamins, and especially folic acid, could be a potential cause of exposure, which is the cause of impaired homocysteine formation [7,30]. Another study from Taiwan [38] found a significant association between the risk of hypertension in people with high exposure and specific genetic polymorphisms, such as *NOS3* G894T, *SOD2* Ala9Val, and *CYBA* C242T. Observations have shown the influence of genetic polymorphisms on As susceptibility through their modulation of As metabolism, detoxification, and DNA repair [4]. In a review of 16 years of literature, sourced equally from across the world's regions, Abhyankar et al. [16] noted an exacerbated hypertension after even a small dose of As in drinking water, although homogeneous and conclusive evidence is lacking. The association of hypertension with constant high exposure to As in groundwater has been reported in people living in an arseniasis-endemic area of Southwestern Taiwan, based on 13 years of observation [39], as well as in Bangladesh [40], Iran [41] and Romania [42]. In a USA cohort study of pregnant women [43], exposure to As in drinking water (up to 147.7 μg/l), was associated with greater monthly increases in systolic blood pressure (SBP) and pulse pressure (PP). Another meta-analysis showed a potential link between chronic As exposure and hypertension [10,44]. As Stea et al. [45] pointed out in their analysis, impact of exposure to As can occur through effects on vascular endothelial cells or through the effects of ROS on endothelial biochemical mediators. The effects of As may reflect cytotoxic effects that cause endothelial dysfunction, potentially resulting in hypertension. There is a strong need for further research, particularly to characterize the etiopathogenic potential of As in causing hypertensive effects on public health.

Atherosclerosis

A study of residents of northeastern Taiwan [46] showed that even low exposure can affect the incidence of carotid atherosclerosis and was correlated with glutathione S-transferase P1 (*GSTP1*) genetic polymorphisms. Further, in high-exposure individuals, a correlation between 1 or 2 *GSTP1* genotypes and p53 variants has already been found. The increased proteinuria in Bangladeshi residents was positively correlated with moderate exposure to As, which may be a manifestation of impaired membranous function leading to atherosclerosis [30,47,48]. Naturally, it seems important to further observe and analyze the negative effects of all forms of As on atherosclerosis, among other things.

Venous insufficiency

Studies in China [18] have shown that a reduction in exposure to this toxic metal over just 1 year can produce significant improvements in peripheral vascular function in men and reverse its effects. A link between As and vascular insufficiency is apparent [6,22]. Thus, further analysis in a multifaceted direction seems to be important to deepen the impact of knowledge of this element's toxicity on venous insufficiency.

Stroke

As is already known, the next leading cause of death among adults is stroke, including in Poland, Europe, and the USA. Nevertheless, direct evidence suggesting impact of long-term exposure to As and ischemic stroke, including mortality, is still lacking [49]. In their study, Tsinovoi et al. [49] confirmed a link between exposure to this toxic element and ischemic stroke. Meanwhile, ecological data confirms its incidence and exposure, with urinary As after ingestion of contaminated water [5,50]. Moreover, data on direct, prolonged, and higher exposure resulting in ischemic stroke is rare. Sometimes As poisoning alone can result in hemolytic anemia, leading to ischemic stroke [13]. Cumulative low-moderate exposure alone, with mean exposure (M = 19.3 μg/l) and mean exposure time (M = 39.5 years), was positively associated with the risk of ischemic heart disease and stroke, increased risk of myocardial infarction, and other cardiac complications [51]. Study patients in Denmark who had been chronically exposed to As (≥10 μg/l) had more strokes overall, including ischemic strokes [52]. Despite the many studies covering the effects of heavy metals, including those of As on CVDs, it is undoubtedly necessary to improve knowledge of the negative effects of all its forms, taking into account stroke.

Ischemic heart disease

Multidimensional analyses conducted in Taiwan [7,53], considering at least a dietary factor, showed a synergistic interaction between ischemic heart disease, which was linked to water consumption and low serum carotene levels. Epidemiological studies described by States et al. [7] showed increased incidence or even occurrence of acute myocardial infarctions in populations with high levels of As exposure and relatively small sample sizes. The literature described by Yuan et al. [54] includes adults and young men, showing the strongest associations among those born during periods of high exposure. This suggests that exposure early in life may increase later cardiovascular risk. Lifetime exposure to As is associated with an increased incidence of myocardial infarction [6]. Meanwhile, Serbia showed an incidence of acute coronary syndrome in areas with lower and higher exposure (1–80 μg/l), where the former had a CVD incidence rate almost twice as high as the latter (124/100 000 and 237/100 000) [55]. Sustained exposure to As alone has been linked to cardiac arrhythmias and is therefore responsible for the increased risk of cardiovascular mortality in humans [4,56]. A cohort study among people in 2 areas in Denmark has already shown the effect of even low exposure to As on myocardial infarction [57]. Tsuji et al. [29] emphasize in their analysis that the collected epidemiological evidence confirmed the association of elevated exposure to As (i.e., >100 μg/l) with CVD, and mainly heart diseases (e.g., ischemic heart disease). Further research is needed to confirm the negative impact of all forms of As on myocardial infarction, a leading cause of death.

Molecular mechanisms of arsenic-induced cardiovascular toxicity

Arsenic and its chemical forms can increase the production of ROS [2,7,58,59]. The exact mechanisms of arsenic's effects on the body are yet to be determined. Its level of toxicity varies depending on the As source, As species, dose, length of exposure, cell/tissue type, and metabolism. The mechanisms of its toxicity include oxidative stress, excessive production of ROS, changes in signaling pathways (e.g., extracellular signal-regulated kinase pathway), etc. [3]. Conversion from As(V) to As(III) and interconversion of As(III) and As(V) produces ROS and reactive nitrogen species and thus disrupts the mitochondrial electron transport chain [4].

Its induction can affect gene expression and trigger various inflammatory responses and homeostasis of endothelial nitric oxide (NO), which is responsible for maintaining vascular tone [5,60,61]. Unfortunately, As in its trivalent form inhibits many other cellular enzymes, if only by binding the sulfhydryl group and altering the phenotype of endothelial cells [17,62]. Endothelial dysfunction underlying CVDs, including hypertension, can be caused by arsenic's effects on the body [7,14,15,18]. Peripheral blood vessels are the main target of as toxicity. High levels of exposure increase arterial stiffness and SBP while lowering diastolic blood pressure (DBP). It worsens the healing of gangrene (blackfoot disease), causing a severe form of peripheral artery disease (PAD). An additional legitimate risk mechanism associated with As and PAD is endothelial toxicity, a precursor leading to the development of vasodilatation and, subsequently, other CVDs [63].

Reduced NO synthase caused by its chronic dysfunction affects numerous physiological or pathophysiological processes. The consequence of this impaired synthase is endothelial dysfunction resulting from the onset of vascular diseases [18,30,38].

A study by Fry et al. [64] confirmed a global change in gene expression in neonatal blood lymphocytes vs. the stress response in neonates exposed to As already in the mother's body. Thus, it becomes quite possible to hypothesize a link between exposure to this toxic element vs. alteration of developmental programming (already at the microRNA [miRNA] stage) and induction of inflammation [2,5,7].

Although As stimulates nicotinamide adenine dinucleotide phosphate oxidase (NOX) enzyme activity, its mechanism is still not fully understood [7]. Nonetheless, a study by Barchowsky et al. [58] showed an increase in endothelial superoxide levels produced by NOX and hydrogen peroxide within 5 min after exposure. The literature data undoubtedly supports the use of vascular NOX in critical molecular pathology analyses of arsenic-related CVD [5,7].

Monomethylarsonic acid (MMA) is repeatedly shown to be associated with stroke, indicating an increase in cytokine expression in lymphocytes [49,65,66]. Further, the Bangladeshi researchers were unsure in their study [49,67] as to the exact interpretation and distribution of the incidence of particular CVDs due to the individual's ability to methylate MMA and later DNA. These 2 major trivalent metabolites, MMAIII and DMAIII, have been linked to CVD and other various adverse health effects [59]. These free radicals have been found to be associated with various DNA-related problems, such as adduct formation, double-strand breaks, cross-linking, DNA mutations and deletions, and chromosomal aberrations [4]. The influence of other external and disruptive substances throughout the body must be considered each

time [8–10,19,28]. This toxic element disrupts immune system function through modulation of oxidative stress, mitochondrial function, and cell signaling, as well as interferes with DNA repair processes, chromosome abnormalities, epigenetic regulation, and apoptosis [2,5,11,68–70]. Arsenic induces oxidative stress in human vascular smooth muscle cells, affecting their antioxidant activity and thus increasing inflammation, promoting endothelial cell growth and apoptosis [4,71]. The epigenetic mechanisms associated with As and its toxic effects include not only DNA methylation and covalent post-translational modifications of histone proteins but involve small non-coding RNAs or miRNAs, in addition to regulating the number of homeostatic and inducible gene expressions [4].

Cohort studies repeatedly show that the efficiency of As methylation can affect the metabolic effects of the methylase-revalase (*As3MT*) gene through oxidative methylation and S-transferase, as well as glutathione through reductive methylation. There is connection between genetic polymorphisms of the *As3MT* gene and the response to toxicity [72,73].

More research is needed to confirm the negative effects of all forms of As on the immune system, already at the molecular and genetic level, which is of great importance for many disorders, including autoimmunity. Further, molecular mechanisms can help understand and produce more advantageous translational tumorigenesis results. A number of other genetic polymorphisms confirm the link between cardiovascular health and exposure to As. There is still a lack of tools to properly identify and verify levels and patterns of epigenetic manifestations, which would allow a full understanding of the epigenetic mechanisms of As cell toxicity [4].

Sources of arsenic in the environment, including in food

Arsenic is found in the environment in the following forms:

- metallic (iAs),
- inorganic (iAsIII and iAsV),
- organic,
- arsine ($AsH3^3$) [4,6,69].

Inorganic As comes in 3 forms:

- red As (As_4S_4 or realgar),
- yellow As (As_2S_3 or orpiment),
- white As (As_2O_3 or arsenic trioxide).

Organic As compounds include:

- methylarsine (CH_3AsH_2),
- dimethylarsine ($(CH_3)_2AsH$),
- trimethylarsine ($(CH_3)_3As$),
- monomethylarsonic acid ($CH_3AsO(OH)_2$, MMAV),
- monomethylarsenous acid ($CH_3As(OH)_2$, MMAIII),
- dimethylarsinic acid ($(CH_3)_2AsO(OH)$, DMAV),
- dimethylarsenous acid ($(CH_3)_2AsOH$, DMAIII),
- trimethylarsinic oxide ($(CH_3)_3AsO$, TMAO),
- tetramethylarsonium ion ($(CH_3)_4As^+$, TMA^+),
- arsenobetaine ($(CH_3)_3As^+CH_2COO^-$, AB),
- arsenocholine ($(CH_3)_3As^+CH_2CH_2OH$, AC), among others [3,4].

Environmental contamination, including with regard to groundwater, is an important public health issue, raised repeatedly at international events. Arsenic occurs naturally in many water sources across the USA, China, India, Argentina, Bangladesh, Cambodia, Chile, Ghana, Taiwan, Pakistan, Vietnam, and Mexico, among others [1,4–6,74].

The most common route of exposure to As is living in areas with high natural concentrations of this element, e.g., in rocks, soil (including agricultural fields), or water [4,12,74].

Arsenic is used extensively due to its properties, e.g., in the industry as an alloying agent, in the production of munitions and preservatives, as well as glass processing, the manufacture of mirrors, metal adhesives, wood preservatives, paper, textiles, or other pigments during skin tanning, other cosmetics, in feed additives, fungicides and pesticides, fossil fuels, inorganic and organic salt, and pharmaceuticals [1,5,6,12,13]. Its natural sources include volcanoes, geysers, and hot springs [5,12,74]. It is estimated that approx. 12 000 tons of As enter or dissolve into the environment each year. The 27 member states of the European Union (EU) produce 3 billion metric tons [12]. Other sources are hazardous waste sites – if the waste has not been properly disposed of and has polluted the surrounding area. Nonetheless, some products no longer contain this ingredient, even though it was used in larger quantities in the past. Currently, its addition is prohibited. Different forms of As can be distinguished (monomethyl arsenic, dimethyl arsenic, arsenobetaine, arsenocholine, arsine gas, arsenic sulfide, arsenopyrite, gallium arsenide), as can various sources of pollution in the environment (including wood) [4,17].

It is worth noting that methyl arsenic is a commonly used organoarsenate-based herbicide that can persist in leaves and soil for a long time. Subsequently, this may pose a serious health risk to people staying in areas where spraying has been carried out [49,75,76].

The most common sources of long-term As exposure are contaminated water from industrial processes, con-

taminated food, mining byproduct, pesticides, chemical waste and smoking (Figure 1) [1,2,6]. Exposure to contaminated food alone is much lower compared to exposure to contaminated groundwater. Most commonly, elevated levels of As occur in such foodstuffs as fish, shellfish, meat, poultry, dairy products, cereals, rice, juices, mushrooms, and fruits. In seafood, As is mainly found in its less toxic organic form [1,4,6,29,49,77]. Some Ayurvedic medicinal products and Indian herbal medicines contained As in their formulation, exceeding the detectable level by almost one-fifth [78]. Ingesting as little as 70–80 mg is fatal to humans [3,79,80]. Its toxicity is highly possibly to be carcinogenic.

The short-term, although intensive exposure/consumption with food of As (30–60 min) can mainly cause various gastrointestinal changes, including a metallic taste in the mouth, burning in the mouth or dysphagia. It can contribute to increased vomiting, brain functions, multi-organ failure, and elevated blood pressure, and further contribute to other symptoms of cardiovascular health (e.g., failure of vital cardiovascular). Such similar symptoms were noticed as early as the 1950s in powdered milk for children. Meanwhile, long-term effect by an investigation mainly concerns high mortality from lung and skin cancers, where the first such symptoms were observed of the British Factory Department in the early 1940s. Even in the early 19th century, numerous skin changes were reported [80].

The WHO estimates that nearly 140 million people have consumed water with As content >10 μg/l. The WHO's proposed limit in water is 10 μg/l [1,4,6,16,18]. Meanwhile, the Environmental Protection Agency has revised its stance, recommending a max level of ≤10 μg/l in the USA [4,6,12,16].

In the past, As was used as a medicinal product and later as the "king of poisons," so its background as a highly poisonous element is quite relevant. Notably, arsenic's toxicity was known earlier, as early as the 13th century. History shows that As played an important, though deadly, role in many conspiracies, whether domestic or wartime ones. It was widely used until methods of detecting it were developed in the 19th century [4].

Inorganic arsenic (in the form of iAsIII as well as iAsV) causes various cancers [3,81]. For a long time, varieties of arsenate were used as medicines, such as Fowler's solution (an alcoholic solution of potassium arsenate) in dermatological, respiratory, and hematological diseases. Salvarsan [82] used it in the treatment of syphilis, pioneering the foundation of modern chemotherapeutics. Organoarsenic compounds were widely used as antibiotics until the 1940s. Today, iAs as arsenic trioxide is used to treat acute promyelocytic leukemia [4,82].

Prevention

In taking preventive measures, especially in areas affected by As contamination, it is essential not only to implement all kinds of measures aimed at protecting citizens' health but to take appropriate action by policymakers and health services, as well as to modernize the industry.

Prevention efforts currently include:

- providing extensive education and raising awareness in schools, workplaces, and healthcare entities,
- using different sources of water, e.g., low-arsenic water for drinking or cooking, and high-arsenic water for washing clothes,
- installing effective As removal systems at a local level,
- reducing occupational exposure across many industrial processes,
- constant monitoring, even at minimal and early poisoning,
- regular sharing of data on government/local websites,
- ending or significantly reducing exposure to contaminated drinking water,
- using special filters with modern nanoarticle technology,
- urgent measures and the latest high-sensitivity analysis methods are needed to protect millions of people around the world from high levels of As in drinking water,
- it is noteworthy that the association between prenatal exposure and the expression of various miRNAs and other biomarkers can be used preventively or as a potential prognostic tool for pathways associated with future cardiovascular pathologies [1,4,6,17,18,31,74].

The problem of occupational exposure in workers involved in the production or use of As is very important. In addition, the use of products containing As (e.g., arsenic-treated wood – chromated copper arsenate treatment) can increase the exposure level (according to Agency for Toxic Substances and Disease Registry) [4].

Any measures taken to implement preventive policies should be selected according to the level of contamination and the source of the element in the selected region. Thus, if there is greater contamination and access in both soil and water then all preventive indications should follow strict guidelines. These could be EU or WHO guidelines, depending on the country's affiliation, or otherwise government guidelines in the case of the USA or selected Asian countries.

Table 1. Recommendations for future research for health protection and environmental action regarding exposure to arsenic (As) [80]

Proposal	Health protection	Environmental action
Future research directions	■ longitudinal studies of cardiovascular diseases morbidity and mortality ■ epidemiological studies on reproductive and pregnancy endpoints ■ identification of vulnerable subpopulations, especially ill people ■ the effect of nutrition on As metabolism and arsenic-induced effects, especially in short-term ■ biomarkers of As exposure and health effects (blood, urine, hair, nails, skin scales) ■ mechanism of action of non-carcinogenic As, as effects of 3 exposures ■ better characterization of As metabolism, including the formation of reactive intermediate metabolites, possible genetic polymorphisms of the enzymatic activities involved and other factors affecting metabolism, including microRNA and DNA ■ characterization of exposure to and bioavailability and toxicity of different as species in foods ■ variation and validation of As levels in the same food products from different geographical areas ■ development of robust, sensitive, accurate and rapid analytical techniques suitable for field measurements of As in water, air and soil	■ global cycling and relative contributions of natural and anthropogenic sources of As in soil, water and air ■ concentration and speciation in as well as effects of As on zooplankton and phytoplankton in estuarine and marine ecosystems and freshwater aquatic systems ■ concentrations of and possible effects of As on terrestrial marine and aerial species ■ the metabolism of inorganic As in seafood, including algae, fish and shellfish

Research perspectives

Unfortunately, few studies refer to low concentrations (<50 μg/l) and even fewer to lower concentrations (<10 μg/l), so further in-depth studies are needed. Another problem is that low concentrations of As in water have been linked to increased SBP, DBP, PP, as well as ischemic heart disease and stroke, which need to be explored further. It seems important to analyze the association impact of exposure to As with various biomarkers and the potential impact of several genome polymorphisms on As methylation under such low doses, considering the potential mechanisms affecting significant changes and CVDs [17]. Meanwhile, it is necessary to understand the relationship between cardiovascular health and As, as well as to understand the mechanisms of action and dose-response relationships (as a biomarker, whether from blood, hair, or urine) [4,7].

There are still no precise guidelines for the rapid analysis of this element, which is why it is essential to develop this field of science and diagnosis. It is only possible to recommend general guidelines for the whole world (Table 1).

CONCLUSIONS

Multi-area studies focused on the effects of As are indispensable, even though the symptoms following impact long-term exposure to iAs vary depending on geographic areas, individuals, and population groups.

Constant exposure and acute poisoning most often lead to blood vessel or heart damage, myocardial infarction, and thickening of the arteries, thereby increasing the risk of CVD and death in humans.

To develop therapeutic strategies, preventive recommendations, and production guidelines against As, it is necessary to immediately implement an integrated study of the environment, conduct a detailed analysis of the exposure data, ensure health surveillance, and examine individual risk characteristics in a specific region of the world. An analysis of all biomarkers will be able to provide mechanistic insights into the pathogenesis of disease processes, including CVDs.

Prospective studies done on a large scale and using reliable biomarkers are required to verify the pathways and causes of the various subunits of CVD. Reducing exposure seems to be very important public health strategy if government assess the impact of this element on cardiovascular health globally.

Even in the case of the smallest and short-term exposure, the toxic and extremely harmful effects of As pose a serious risk of at least cardiovascular health, which is a major public health challenge worldwide. It is absolutely necessary to develop capabilities for rapid diagnostics and analysis of As under various conditions.

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