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Environmental toxicology of arsenic to wildlife (nonhuman species): Exposure, accumulation, toxicity, and regulations

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29.1 Introduction

Arsenic (As) is a ubiquitous metalloid found in all environmental compartments, making exposure of humans and nonhuman species to arsenic through the air, water, or diet a common phenomenon. Arsenic is released into the environment primarily in its inorganic from both natural and anthropogenic sources elevating its concentration in terrestrial and aquatic ecosystems, with the latter often being its ultimate sink. Arsenic does not degrade in the environment, and it is a highly bioaccumulative and toxic element. Arsenicosis (chronic illness from toxic arsenic exposure) and acute arsenic toxicity in humans is reported globally and affects almost 500 million people in over 107 nations [1]. Consequently, arsenic is one of the most extensively investigated elements in the last 20 years and is regarded as a hazardous substance of priority by US Agency for Toxic Substances and Disease Registry [2]. In contrast to its well-documented effects in humans, the knowledge for arsenic exposure and toxicity in nonhuman species especially wildlife is limited, essentially due to a lack of understanding of the symptoms specific to arsenic toxicity and its mode of toxic action in nonmammalian species. Although scientific literature provides some evidence of chronic arsenic intoxication in feral and domesticated animals [3–6]. The arsenic toxicity in the environment can be profoundly influenced by its chemical speciation and the route of exposure. In aquatic ecosystems, organisms can be impacted by arsenic via direct exposure from water as well as its trophic transfer through the aquatic food web. This chapter mainly focuses on current understanding of the source of exposure, chemical speciation, uptake and bioaccumulation, and adverse biochemical and physiological effects of arsenic in nonhuman species.

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29.2 Sources of arsenic and its concentration in contaminated systems

Arsenic is primarily deposited in the lithosphere and enters the atmosphere via natural and anthropogenic processes (Fig. 29.1). Natural processes of arsenic contamination in the environment include weathering of rocks, geothermal, and volcanic activities. Usual background arsenic concentrations in the freshwater range between 0.01 and 2 $\mu g L^{-1}$, and ecotoxicologically relevant contamination of surface waters with no anthropogenic input of arsenic is a rarity [7,8]. Nonetheless, rivers and lakes with their headwaters in arsenic-rich beds may contain significantly high concentrations of arsenic. For example, the Chilean rivers flowing through volcanic sediments can have arsenic concentration exceeding 2000 mg As L^{-1} [9,10]. On the other hand, the main anthropogenic sources of arsenic contamination in the environment include mining and burning of fossil fuels. Arsenic comes as a by-product of gold and coal mining. In addition, arsenic is mined and extracted from mineral ores for its use in various modern purposes, such as electronics industry, batteries, paints, wood preservatives, pesticides, and pharmaceuticals [11]. Water bodies that

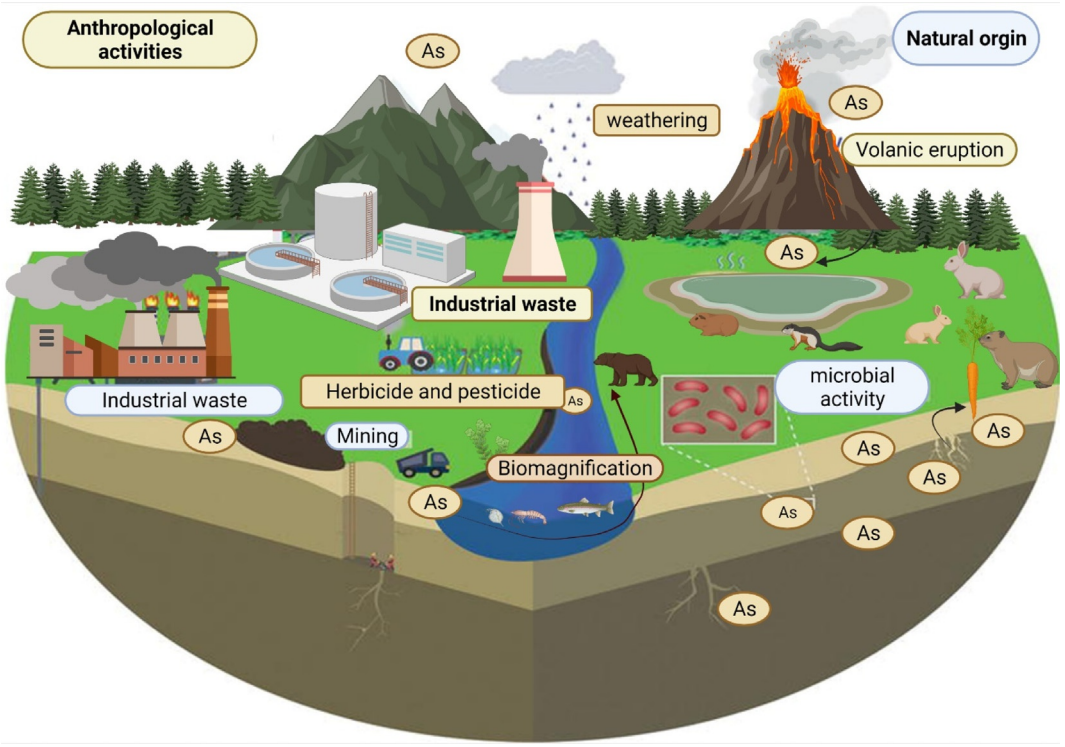

FIG. 29.1 Natural and anthropogenic sources of arsenic contamination in the environment and its exposure to wildlife.

receive mining and industrial effluents often have elevated arsenic concentrations that can cause detrimental health effects in resident species. For example, industrial contamination of Maurice River (NJ, USA) caused arsenic concentrations to reach 4100 $\mu g L^{-1}$ [12]. Similarly, arsenic concentrations as high as 583 and 18,910 $\mu g L^{-1}$ in the surface water were reported from the mining district of Ron Phibun in Thailand and Obuasi in Ghana, respectively [13,14]. Mining activities can also lead to highly elevated levels of arsenic in the soil and vegetation in surrounding terrestrial systems. For example, arsenic levels in the range of 75–400 and 22–725 $mg kg^{-1}$ dw in surface soil and vegetation, respectively, have been reported near the vicinity of Giant Mine (a decommissioned gold mine), Yellowknife, Canada, in comparison to arsenic levels of 1–10 and 0.001–0.6 $mg kg^{-1}$ dw in respective environmental matrices from reference areas [15,16].

29.3 Speciation of arsenic in the environmental compartments

In the environment, arsenic mainly occurs in four oxidation states: arsenate (+V), arsenite (+III), elemental arsenic (0), and arsine (-III). Arsenite and arsenate are the only oxidation states found in living organisms, while elemental arsenic and arsine are found rarely and only occur in extremely reducing conditions. Inorganic forms of arsenic are more soluble than its organic forms and therefore are readily absorbed by organisms. Once accumulated, inorganic arsenic is reduced and converted to methylated arsenicals, arsenobetaine, arsenocholine, trimethylarsine, and arsenosugars by the organisms [17].

29.3.1 Freshwater

Under oxic conditions, arsenate is the most predominant state; however, arsenite can dominate under reducing conditions, such as aphotic zones of deep lakes, and nutrient-rich eutrophic lakes. Reduction of arsenate to arsenite increases the mobility of arsenic [8,18]. In addition to the redox potential of the water, other processes, such as sorption, adsorption, precipitation, and biological transformation, may influence the conversion of As(V) to As(III) [8,17].

29.3.2 Saltwater

Similar to the freshwater, arsenic also occurs in four oxidation states of arsenate, arsenite, elemental arsenic, and arsine in estuaries and oceans. Arsenate is the predominant oxidation state in the well-oxygenated layers. The As(V)-to-As(III) ratio is low (0.1:1 to 10:1) in the deeper oceanic zones, in comparison to the theoretical thermodynamic calculations (1026:1) [17]. In addition to arsenite and arsenate, methylarsonate and dimethylarsinate are detected in the seawater and interstitial waters of the oceans [19]. The phytoplanktonic methylation of inorganic forms of arsenic could be a major contributor to the presence of methylated forms of arsenic in seawater [20].

29.3.3 Soil

The average concentration of arsenic in Earth's upper crust is estimated between 1.5 and 2.0 μg/kg [21]. Arsenic in the crust is generally present as a natural constituent of sulfide minerals, in the form of X(*II*)AsS, where X represents a bivalent metal, such as Fe, Ni, and Co [22]. Arsenic in the soil occurs in both inorganic and organic forms (species). The most common inorganic species are arsenate (AsV) and arsenite (AsIII), while the most common organic species are monomethylarsonic acid (MMA) and dimethylarsinic acid. The arsenic speciation in soil depends on its texture, organic matter content, pH, and redox potential. Under aerobic conditions, arsenate is the most common species, which has limited mobility as it is adsorbed by clay particles and organic matter or exists as oxides or hydroxides of iron or manganese [23]. However, under anerobic conditions, arsenate is reduced to arsenite, which is highly mobile and readily available for uptake by plants and invertebrates living in the soil (Fig. 29.1).

29.4 Bioaccumulation of arsenic

29.4.1 Exposure routes and uptake mechanisms

Dietary uptake is generally the predominant route of exposure in terrestrial animals; however, branchial uptake is also prominent in aquatic organisms, such as fish. The relative importance of diet or waterborne exposure in wildlife is complicated by many confounding variables, such as the arsenic speciation, animal species and life stage, and exposure duration. For example, it was demonstrated in rainbow trout that endpoints of chronic toxicity, such as reduced growth rate, are correlated to arsenic burden in tissues that are reflective of dietary intake. In contrast, fish mortality is a more sensitive endpoint during waterborne arsenic exposure [24].

29.4.2 Gastric uptake of arsenic

Arsenic uptake in the intestine is carrier mediated [25,26]. Both in vitro and in vivo mammalian studies indicate that intestinal organic anion-transporting polypeptides, aquaporins (AQP10), and glucose transporters (GLUT5) have major role in the uptake of As(V), whereas As(III) uptake is believed to be mediated by phosphate transporters [26,27]. The aquaglyceroporins were also implicated for gastric uptake of As(III) and monomethylarsonous acid (MMA III) in zebrafish [25]. Organisms at the bottom of the food chain can also uptake inorganic arsenite from the environment and biotransform it within their bodies into organic and methylated arsenicals. Thus, when organisms occupying higher trophic levels consume organisms below them in the food web, they are exposed to both inorganic and organic species of arsenic. However, the rate of accumulation of inorganic arsenic from diet still exceeds that of the organic arsenicals [28].

Recent studies indicate that the gut flora may influence the absorption of arsenic and its speciation across the intestine. Gut flora may influence the redox balance in the

intestinal lumen through enzymatic or nonenzymatic secretions. Furthermore, some gut microbes may even sequester arsenic or change the expression of transporters involved in arsenic transport across the intestinal epithelium [29]. Microbes may also biotransform arsenic in the food to less toxic arsenobetaine [30]. Modification of gut flora is relatively easier in domesticated and commercial animals through treatment with probiotics, which is a scenario that does not occur in wild animals and thus potentially make them more susceptible to arsenic exposure in the environment.

29.4.3 Branchial uptake of arsenic in aquatic organisms

The branchial absorption is the predominant route of accumulation of waterborne arsenic in fish and many other aquatic organisms. During chronic exposure, the uptake of waterborne arsenic across the fish gill demonstrates a saturable kinetic pattern with a linear increase in the beginning which eventually reaches a steady state [31]. A bioconcentration factor (BCF; ratio of arsenic in tissues and ambient water) ranging from 1.6 to 3.2 for inorganic arsenic has been reported in tissues, such as gill, liver and stomach for arsenic(V) and arsenic(III) in Nile tilapia (*Oreochromis niloticus*) [31–33]. A BCF of ~96 was also reported in the muscle of fish captured from sites impacted by mining effluents [34]. The mechanisms of branchial arsenic uptake are currently poorly understood. However, AQP (aquaporin) present in the chloride cells of the gills has been implicated in branchial absorption of arsenic [35]. There is a complete lack of information on the mechanism of arsenic uptake in fauna at the bottom of the trophic chain. However, it has been reported that phosphates could reduce arsenic uptake in earthworms (*Eisenia fetida*) [36]. Since arsenate and phosphate are structurally similar [8], this result is not surprising and could indicate a possibility of phosphate transporters being involved in dissolved arsenic uptake in aquatic organisms, such as oligochaetes and fish.

29.4.4 Trophic transfer of arsenic

The trophic transfer of arsenic is an important aspect of biogeochemical cycling of arsenic, especially in the aquatic systems [37]. In the aquatic food web, primary producers can absorb inorganic arsenic and transfer it to higher trophic level organisms (grazers and carnivores). The accumulation and trophic transfer of arsenic is a function of organismal uptake and the rate of excretion and can be influenced by arsenic speciation in the environment and as biotransformation processes in the [38–40]. Several studies suggested higher accumulation of arsenic in predator species, which indicates efficient trophic transfer of arsenic [40–42]. Macroinvertebrates that form an important component of aquatic food chain and nutrient cycle are known to be more sensitive to waterborne arsenic relative to fish and other aquatic species [38]. However, multitrophic studies indicate biodilution of arsenic along the food chain, despite its higher accumulation at the base of the trophic chain [39,43]. In contrast, study demonstrated that higher arsenic accumulation in herbivorous fish, which suggests that foraging behavior could be an important determinant of the efficiency of trophic arsenic transfer of arsenic [40]. Despite evidence

of biodilution of arsenic at the higher trophic levels, fish that directly feed on macroinvertebrates with elevated arsenic body burden could experience considerable risk to arsenic toxicity [32]. Reports of trophic transfer of arsenic from soil to plants, and to the herbivorous terrestrial mammals, also exist [5,6,15,44].

29.4.5 Tissue specific distribution of arsenic

Lack of specific biomarkers to assess adverse effects of arsenic exposure in wildlife is a major impediment in ecological risk assessment. In the real world, where organisms are often exposed simultaneously to multiple contaminants, lack of arsenic-specific biomarkers makes it difficult to establish a strong linkage between arsenic exposure and its pathophysiology in impacted organisms. Furthermore, the current literature is inconsistent on the exposure concentrations of dietary or waterborne arsenic that would result in chronic toxicity in organisms. Nevertheless, arsenic is known to accumulate in multiple organs in aquatic organisms, such as fish, and the pattern of accumulation is influenced by the exposure route (Table 29.1). For example, gill becomes a key organ for arsenic accumulation during waterborne exposure to arsenic, whereas intestine becomes a critical organ of arsenic sequestration during dietary exposure. Irrespective of exposure route, significant arsenic accumulation also occurs in other target organs, such as liver, kidney, muscle, and brain, in fish during chronic exposure to arsenic [50–52].

Uptake, absorption, distribution, biotransformation, and excretion determine arsenic tissue burden. For example, gill and liver accumulate the highest amount of waterborne arsenic in fish [45,46], and dietary arsenic is most abundantly present in the intestine, pyloric caeca, and liver in fish (Table 29.1) [48,49,51,53]. Mammals are known to sequester arsenic in exoskeletal protein, making skin and nails effective bioindicators of arsenic exposure [5,6,15]. Birds usually excrete a large amount of arsenic through feces. However, a significant proportion of arsenic may still remain in the blood that is eventually

Table 29.1 Tissue-specific distribution of arsenic in various fish species.

Fish species	Exposure route	Accumulation of arsenic in fish organs	References
Danio rerio	Waterborne	Liver > gills > muscles > heart > intestine > eye > skin > brain	[25]
Clarias batrachus	Waterborne	Liver > gills > blood > muscles > skin > brain	[45]
Labeo rohita	Waterborne	Liver > gills > kidney > gut > bones > skin > muscles > scales > fins	[46]
Cirrhinus mrigala	Waterborne	Liver > kidney > gills > gut > skin > scales > bones > muscles > fins	[46]
Catla catla	Waterborne	Gills > liver > kidney > gut > bones > skin > muscles > scales > fins	[46]
Clarias gariepinus	Waterborne	Muscles > liver > gills > bone > gut > fins	[47]
Tilapia zilli	Waterborne	Liver > muscle > gut > gills > bone > fins	[47]
Coregonus clupeaformis	Dietary	Pyloric caeca > liver > intestine > gallbladder > kidney > stomach > scales > skin	[48]
Cyprinus carpio	Dietary	Intestine > bone > gills > liver > muscle > brain	[49]

deposited in the liver, feathers, and eggs [54,55]. Deposition of arsenic in eggs is of great ecological concern, especially for migratory birds. Insectivorous migratory birds often feed voraciously to meet their high energetic demands of flight and breeding, accumulating a significant amount of arsenic and depositing it in their eggs, putting the embryo at risk of arsenic toxicity [55].

The metabolically active forms of arsenic in target tissues, rather than total arsenic tissue burden, are more reliable indicators of its toxic effects. Interestingly, the arsenic body burden associated with its chronic exposure, irrespective of the route, has been suggested to be similar among different fish species [17]. An arsenite body residue of 1.93 $mg\,kg^{-1}$ has been reported to cause a 10% reduction in the growth rate of tilapia [56]. Similarly, 2.24 $mg\,kg^{-1}$ of dietary arsenic(III) in bluegill sunfish and 2–4 $mg\,kg^{-1}$ of arsenic(III) and 4–6 $mg\,kg^{-1}$ of arsenic(V) in rainbow trout were associated with significant reduction in growth and survival during chronic exposure to arsenic [57–59]. Chronic exposure to dietary arsenic(III) that elicited toxic effects also resulted in 2–6 μg of arsenic burden per g of renal and hepatic tissues in rainbow trout [51].

Similar tissue-specific distribution has also been found in birds and mammals during environmental exposure to arsenic, with intestine, liver, kidney, and lungs being the major sites arsenic accumulation [54,55]. Moreover, significant arsenic deposition has been reported in bones and nonliving tissues, such as hair and nails in multiple wild mammalian species living in arsenic contaminated environments [5,6,15,44]. Arsenic deposition in hairs, feathers, and nails could be an efficient strategy for sequestration and eventual elimination of arsenic from the body, which also suggest their usefulness in assessing arsenic exposure in wildlife.

29.5 Mechanisms of arsenic toxicity

As in humans, toxicity of arsenic in nonhuman species is also dependent on its chemical species and oxidation state. Generally, inorganic forms of arsenic are more toxic than their organic complements. Furthermore, arsenite (As-III) is more toxic than the arsenate (As-V) [60]. Since arsenic bears chemical resemblance with phosphorus, it may uncouple synthesis of ATP synthesis or replace phosphorus on active sites of enzymes and thereby impair metabolism [17,61]. However, most serious implications of arsenic intoxication are usually attributed to oxidative stress which can damage various cellular macromolecules, such as enzymes, lipids, and nucleic acids [51,62–64].

29.5.1 Oxidative stress

Arsenic is known to induce oxidative stress by facilitating the production of reactive oxygen species (ROS) or through weakening of the antioxidant response [65]. It has been suggested that inorganic arsenic (e.g., As-III) induces generation of superoxide molecules through the activation of NAD(*P*)H oxidase [66] or by affecting the nitric oxide (NO) synthase enzyme system [67]. In addition to ROS generation, As-III was found to facilitate

oxidative stress by suppressing the cellular redox mechanisms. For example, chronic environmentally relevant dietary exposure to arsenite to rainbow trout (*Oncorhynchus mykiss*) was found to reduce cellular thiol redox (oxidized to reduced glutathione ratio) and increase lipid peroxidation in the liver [51]. Moreover, chronic exposure to arsenite was found to upregulate the activities of hepatic enzymatic, such as catalase, superoxide dismutase, and glutathione peroxidase, likely as a compensatory response to increased hepatic ROS generation [51].

29.5.2 DNA damage

DNA is a common target of oxidative damage, and arsenic-induced oxidative DNA damage is well characterized [68]. Arsenic is known to cause many types of DNA damage including lesions and strand breaks, as a result of increased oxidative stress [69]. Arsenic exposure causes hydroxy radicals to react with DNA nucleobases, resulting in DNA lesions and formation of adducts, such as 8-hydroxy-2′-deoxyguanosine, 5-hydroxycytosine, and 5-hydroxyuracil [67]. Laboratory-based studies on mammals indicate that As exposure can affect cell cycle and interfere with the transcription of genes related to DNA repair and thereby induce carcinogenesis [70]. A cell with significant damage to its DNA usually proceeds toward apoptosis; however, altered cell cycle pathways, altered DNA repair mechanism, and activation of proinflammatory pathways help arsenic-exposed cells to survive, which could promote carcinogenesis. Likewise, arsenic alters the expression of apoptosis-regulating proteins, such as Bax (proapoptotic) and Bcl2 (antiapoptotic), despite increased DNA damage [71]. Although arsenic-induced ROS were shown to generate DNA adducts, DNA strand breaks, and also chromosomal aberrations with crosslinks [70], it has been suggested that arsenic does not interfere directly with DNA [72].

29.5.3 Neurodegeneration and neuronal dysregulation

Arsenic is believed to cause structural and functional damage to the central nervous system by several different mechanisms, which are not yet fully understood. These mechanisms include: (i) mitochondrial dysfunctions and oxidative damage in various cells including the neurons in the brain; (ii) demyelination and abnormal myelination leading to impaired structural and functional maturation of the brain, especially at early life stages; and (iii) disruption of multiple neurotransmitters signaling pathways in the brain including dopamine, serotonin, gamma aminobutyric acid, glutamate, and NO (see [73] for review). Collectively, these perturbations can adversely affect a wide range of brain functions including brain plasticity, motor and sensory dysfunctions, and cognition and memory functions. Much of the current knowledge on the arsenic neurotoxicity is based on human and rodent studies, as arsenic neurotoxicity has rarely been investigated in any wild species.

29.5.4 Epigenetic dysregulation

Environment epigenetics is a fast-growing field that concerns the effects of environmental contaminants on the epigenetic make up of organisms. DNA methylation, histone

modification, and noncoding RNAs are examples of epigenetic modifications to genomes that do not involve changes in DNA sequences. Arsenic-induced changes in the DNA methylation patterns on CpG islands of the promoter region of the genome are often associated with human diseases. Lately, with the advancement of environmental epigenetics, arsenic-induced changes in DNA methylation pattern have been demonstrated in nonhuman species, such as mice and zebrafish [74,75]. Interestingly, altered methylation patterns following arsenic exposure have been associated with aberrant cognitive and behavioral patterns and improper organogenesis [76].

Arsenic has been suggested to dysregulate or alter epigenetic marks to induce malignancies (States, 2015). Current evidence strongly indicates the role of noncoding microRNAs (miRNAs) in arsenic-induced dysregulation of cell cycle and proliferation [77]. Arsenic has also been reported to influence the expression of miRNA-135b in killifish (*Fundulus heteroclitus*), potentially affecting various cellular functions, such as osmoregulation, cell migration, and organelle assembly [78]. The miRNAs regulate the expression of genes by base pairing with the target mRNAs, and they have multiple roles in many physiological processes including organogenesis, immunity, and brain functions [79]. Like the noncoding miRNAs, posttranscriptional changes to histone proteins, particularly in the histone tail region of nucleosomes, can also change the way a DNA double helix interacts with the gene transcription machinery, thereby facilitating or silencing certain regions of the genome. For example, the polycomb repressive complex 2 catalyzes the tri-methylation of histone H3's lysine 27 (H3K27me3), which silences genes [80]. A recent study demonstrated that low doses of inorganic arsenic can increase the methylation of histone H3K4me3 in the nervous system of zebrafish (*Danio rerio*), which could have implications on its motor and cognitive functions [81]. Moreover, the histone modifications were transgenerational, suggesting that this could be an important mechanism for the transgenerational toxicity of arsenic.

29.6 Toxic effects of arsenic

Much of current information on the toxic effects of arsenic in situations of environmental or ecological concern is focused on aquatic organisms, mainly fish, while studies on arsenic toxicity in other wildlife species including birds and mammals are extremely limited. This section provides a summary of the acute and chronic toxicity of arsenic in various species.

29.6.1 Acute toxicity

Acute toxicity of arsenic has been mostly studied with inorganic arsenic (arsenite or arsenate), and arsenite has been found to be ≥2-fold toxic to aquatic organisms than arsenate (Table 29.2). In fish, adults are generally more tolerant to arsenic than the larvae or juveniles. For example, the 96-h LC_{50} of arsenic in adult fish usually exceeds 20 mg L^{-1}, whereas it varies between 5 and 10 mg L^{-1} in larval and juvenile fish (Table 29.2).

Table 29.2 Toxicity of inorganic arsenic in different fish and aquatic invertebrates.

Fish species	Common name	Life stage	Arsenic species	Exposure duration (hours)	LC50 (mg As L^{-1})	References
Rhinella arenarum	South American toad	Embryonic and juvenile stage	Arsenite	168	24.3	[82]
Catla catla	South Asian carp	Fingerlings	Arsenite	96	20.41	[46]
Channa punctatus	Spotted snakehead	Fingerlings	Arsenite	96	10.8	[83]
Chanos chanos	Milkfish	Fingerlings	Arsenite	96	7.29	[84]
Xyrauchen texanus	Razorback sucker	Fry	Arsenate	96	17.8	[85]
Labeo rohita	Rohu	Juvenile	Arsenite	96	28.3	[46]
Chelon labrosus	Thicklip gray mullet	Juvenile	Arsenite	96	27.3	[84]
Danio rerio	Zebrafish	Juvenile	Arsenate	96	43	[86]
Lepomis macrochirus	Bluegill	Juvenile	Arsenite	96	17.3	[87]
Lepomis macrochirus	Bluegill	Juvenile	Arsenite	96	17.3	[87]
Thymallus arcticus	Arctic grayling	Juvenile	Arsenite	96	5.5	[88]
Oncorhynchus mykiss	Rainbow trout	Juvenile	Arsenite	96	91	[88]
Oncorhynchus shawytscha	Rainbow trout	Juvenile	Arsenite	96	21.4	[88]
Pimephales promelas	Fathead minnow	Juvenile	Arsenite	96	12.6	[89]
Cirrhina mrigala	Mrigal carp	Adult	Arsenite	96	24.5	[46]
Ctenopharyngodon idella	Grass carp	Adult	Arsenite	96	22.17	[46]
Labeo rohita	Rohu	Adult	Arsenite	96	30	[46]
Channa punctatus	Spotted snakehead	Adult	Arsenate	96	42	[83]
Clarias gariepenus	African sharptooth catfish	Adult	Arsenite	96	89	[90]
Anabus testudinus	Climbing perch	Adult	Arsenate	96	18.21	[91]
Oreochromis mosambicus	Mozambique tilapia	Adult	Arsenite	96	28.68	[92]
Catla catla	South Asian carp	Adult	Arsenate	96	43.78	[93]
Limanda limanda	Common dab	Adult	Arsenite	96	28.5	[94]
Cyprinus carpio	Eurasian carp	Adult	Arsenite	96	32	[95]
Hyalella curvispina [96]	Amphipod	Adults	Arsenite	96		1.76–2.14

Mardirosian et al.(2015) studied acute toxicity of arsenic in different embryonic stages of common South American toad (*Rhinella arenarum*) and reported an average 4–8 day LC_{50} of 24.3 mg L^{-1} [82]. The available acute toxicity data also indicate that aquatic invertebrates, such as daphnids, copepods, and amphipods, are more sensitive to arsenic than fish or amphibians (Table 29.2). It is important to note that animals often develop

tolerance to arsenic during acute exposure. For example, zebrafish exposed to arsenate at concentrations of 5–15 mg L^{-1} showed greater mortality within the first 48 h, but fish that survived were able to tolerate much higher arsenic concentrations in the next 48 h with minimal mortality [97]. After initial exposure, the increased tolerance to arsenic could result from adaptive physiological responses, including upregulated detoxification and elimination processes.

29.6.2 Chronic toxicity

Chronic toxicity of arsenic typically occurs in animals in the form of growth depression, impaired reproductive performance, and altered behaviors (Fig. 29.2).

29.6.2.1 Effects of arsenic exposure on growth

In fish, growth has been suggested to be a more sensitive endpoint than survival during chronic exposure, and growth suppression in early life stages occurs around the same exposure levels that cause acute toxicity during waterborne exposure [17]. Similar to acute exposure, animals can also produce compensatory adaptive response during chronic exposure by upregulating biotransformation and excretion of accumulated arsenic, however, that typically entails energetic cost and growth depression occurs as a tradeoff [98]. Chronic exposure to environmentally relevant concentrations of both dietary and waterborne arsenic has been found to reduce growth in fish, which was associated with elevated arsenic body burden (Table 29.3) [28]. Growth depression in fish exposed to arsenite via water is generally observed at concentrations >1 mg L^{-1} (Table 29.3) [17]. It is important to note that during chronic exposure to arsenic, growth reduction is predominantly observed in animals during the phase of active growth, such as the larval or juvenile stages, whereas

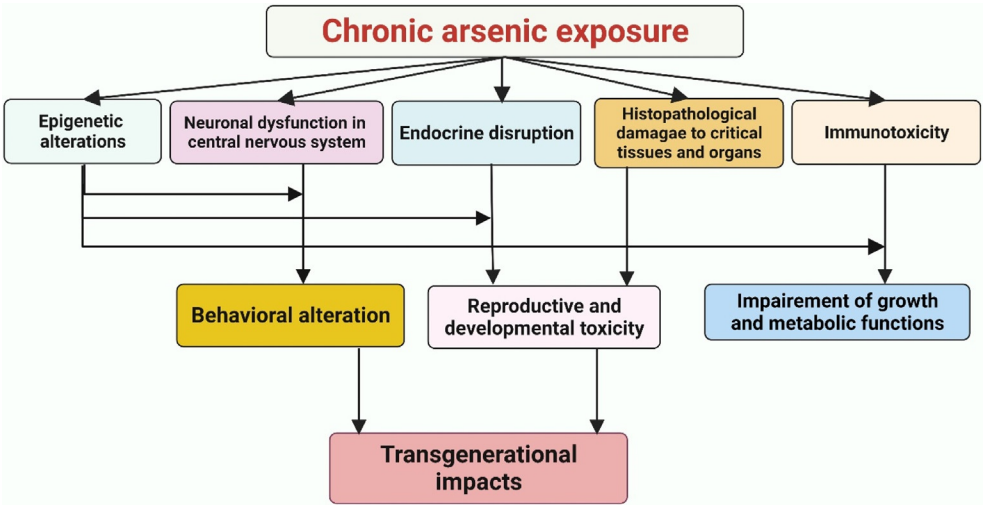

FIG. 29.2 Pathways of toxicity in animals during chronic exposure to arsenic.

Table 29.3 Toxic effects of chronic arsenic exposure in different nonhuman species.

Organism	Arsenic speciation	Effect	Reference
Growth effects			
Rainbow trout	Arsenite	Exposure to juvenile fish shows that strong reduction in growth and increased accumulation and mortality	[24]
Fathead minnows	Arsenite	Increased wholebody arsenic accumulation and decreased growth rate and survival	[38]
Rainbow trout	Arsenite	Increased arsenic accumulation in liver, kidney, and muscle and reduction in body weight to length ratio	[51]
Goldfish	Arsenite and arsenate	Increased arsenic accumulation in muscle and reduced growth	[98]
Hepatic and nephrotoxic effects			
Gilthead seabream	Arsenic trioxide	Hypertrophy, vacuolization, and cell death in liver	[99]
Aquatic birds, such as cattle egret, indian pond heron, and terrestrial birds bank myna spotted owlet	Arsenite	Increased arsenic accumulation in liver and kidney causing significant oxidative stress	[100]
Zebrafish	Arsenite	Compromised innate immune response, and marked increase in viral and bacterial load in embryos	[101]
Indian major carp	Arsenic trioxide	Increased hepatic tissue damage, alanine aminotransferase activity, and increased mortality	[102]
Walking catfish	Arsenite	Immunosuppressive effect, death of head kidney macrophages. Increased hemosiderin accumulation, decreased melano-macrophage count	[103]
Reproductive effects			
Zebrafish	Arsenite	Reduced cumulative egg production, decreased hatching rate in embryos	[104]
Rat	Arsenite	Endocrine disruption via altered estrogen signaling pathway	[105]
Mud minnow	Arsenite	Declined hatching success and impaired growth, muscle fiber density, and diameter	[106]
Zebrafish	Arsenite	Increased mortality in embryos Delayed and deformed embryo development	[107]
Chicken	Arsenic trioxide	Reduced body weight, also declined egg production and egg weight, and increased embryonic mortality	[108]
Chicken	Arsenic trioxide	Increased inflammation and testicular toxicity Negative impact on testicular development	[109]
Rat	Arsenite	Significantly decreased weight of the testis, impaired sperm motility and morphology	[110]

Table 29.3 Toxic effects of chronic arsenic exposure in different nonhuman species—cont'd

Organism	Arsenic speciation	Effect	Reference
Behavioral effects			
Mozambique tilapia	Arsenite	Abnormal anxious behavior	[92]
Asian clam	Arsenite	Behavioral alteration in valve movement response	[111]
Zebrafish	Arsenite	Impaired long-term memory and increased protein oxidation in brain	[112]
Rat	Arsenite	Abnormal structural changes in myelin sheath hippocampal region nerve fibers, also impaired spatial memory	[113]
Mouse	Arsenate	Perinatal exposure induced depression and depression-like behaviors in offspring. Also, disruption of hypothalamic–pituitary–adrenal axis, and the serotonergic signaling in the dorsal hippocampal region	[114]
Mallard ducklings	Arsenite	Behavioral changes including increased resting time and decreased alert behavior	[115]

animals that have either reached their full growth potential or a slower growth rate may not necessarily exhibit any suppression of growth. Moreover, fish morphometrics is often a better indicator of general health status than growth rate during chronic arsenic exposure. For example, chronic exposure to dietary arsenic (80 $\mu g\,As\,g^{-1}$ dry weight; as arsenite) significantly reduced the condition factor (ratio of body weight to length) in rainbow trout without affecting their growth rate relative to control fish [51].

29.6.2.2 Hepatotoxic and nephrotoxicity from arsenic exposure

Liver is the primary site of arsenic accumulation and biotransformation in vertebrates [116]. Chronic exposure to arsenic in aquatic and terrestrial vertebrates is often associated with hepatic steatosis (fatty liver) and abnormal hepatic histopathology, such as hypertrophy, vacuolization, and apoptosis of the hepatocytes (Table 29.3) [92,99]. Significant accumulation of arsenic also occurs in the kidney during chronic exposure resulting in nephrotoxicity in exposed organisms [55,100]. Arsenic-induced oxidative damage is likely to be the main driver of structural and functional impairment of liver and kidney during chronic exposure [117]. In addition, an increased rate of renal filtration to remove arsenic from the body may also overwhelm the kidney reducing its functional efficiency [118].

29.6.2.3 Immunotoxicity of arsenic

Chronic exposure to arsenic even at extremely low concentrations has been reported to impair innate immune response and cause immunotoxicity in several fish species (Table 29.3). Exposure to 2–10 $\mu g\,L^{-1}$ arsenic (As-III), which is considered safe in drinking water for human consumption, was found to cause a marked increase in viral and

bacterial load in embryonic zebrafish. This increase in pathogen load was essentially resulted from the decline of antiviral and antibacterial cytokines following arsenic exposure [101]. In Indian catfish (*Clarias batrachus*), exposure to ~75 μg L^{-1} arsenite for 30 days led to a significant accumulation of arsenic in head kidney, and the death of head kidney macrophages (HKMs), thereby decreasing the capacity to fight off pathogenic infection. The death of the HKMs was triggered by the activation of caspace-3-mediated apoptosis, which occurred due to arsenic-induced oxidative stress in the head kidney [103]. Chronic waterborne exposure to inorganic arsenic (As-III) was also found to induce apoptotic cell death and immunotoxicity in marine species, such as European sea bass (*Dicentrarchus labrax*) [119].

29.6.2.4 Reproductive toxicity of arsenic

The increased energetic cost invoked by the arsenic detoxification and excretion may not only affect growth but also compromise the reproductive performance of both males and females during chronic exposure (Table 29.3). In fish, fertility has been suggested to be one of the most sensitive endpoints of chronic waterborne exposure to inorganic arsenic above 1 mg L^{-1} [120]. Zebrafish breeding pairs fed with arsenic-contaminated wild polychaete worms (*Nereis diversicolor*) showed a 47% decrease in cumulative egg production and a 36% decrease in spawning frequency relative to fish fed with uncontaminated worms. The decrease in egg production in this study was associated with decreased expression of vitellogenin gene in the liver of females, suggesting reduced vitellogenesis [104]. Inorganic arsenic is believed to interfere with hypothalamus-pituitary-gonadal axis, which can disrupt estrogen signaling pathways in females [105]. Exposure to inorganic arsenic has also been suggested to inhibit 11-ketotesterone synthesis and spermatogenesis in male fish [121,122]. Consistent with these observations, hatching success was decreased when both male and female zebrafish treated with dietary arsenite were paired with members of opposite sex who were treated with uncontaminated diet (unpublished data). Reproductive toxicity of arsenic is also well documented in mammalian models and possibly occurs in birds as well [123,124].

29.6.2.5 Neurobehavioral effects of arsenic

As described in the previous section, arsenic is a neurotoxicant and can cause behavioral alterations in animals by disrupting neural networking and neural signaling pathways in the brain (Table 29.3). Behavioral effects of environmental contaminants are much less studied in wildlife; however, the effects can be subtle and yet have profound implications for their survival and long-term sustenance in the natural environment. Chronic exposure to inorganic arsenic (As-III) affects a wide variety of animal behaviors, such as learning and memory, anxiety-like behaviors, social behaviors, and motor function, which are well documented in rodents (see [73] for review). Alterations in many of the similar types of behavior were also recently reported in adult zebrafish exposed to 50–500 μg L^{-1} arsenite that spanned from 4 h to 150 days postfertilization [125]. The underlying mechanisms of arsenic-induced behavioral alterations in nonmammalian organisms have rarely been investigated; nonetheless, recent investigations indicate that cognitive dysfunction in

zebrafish chronically exposed to arsenite likely is mediated by oxidative stress and disruption of dopaminergic signaling in the brain (unpublished data).

29.6.2.6 Developmental and transgenerational effects of arsenic

Arsenic is transferred from the mother to the eggs via egg yolk in oviparous animals, such as fish and birds [126,127], which can cause developmental toxicity in offspring. The developmental effects of placental transfer of arsenic in mammalian models like rodents are well characterized, but it has rarely been investigated in nonmammalian species. Direct embryonic exposure to arsenite (37–750 $mg\,L^{-1}$) reduced larval survival and caused multiple developmental abnormalities including pericardial edema, and cardiac and spinal cord malformation [128]. The mechanistic underpinnings of these developmental effects are currently not known but may involve epigenetic mechanisms, such as abnormal genomic DNA methylation pattern. A recent study also documented the transgenerational behavioral effects of exposure to inorganic arsenic in zebrafish [81]. Exposure to waterborne arsenite (50–500 $\mu g\,L^{-1}$) altered motor activity and increased anxiety-like behaviors in parental generation (F0), which were transmitted to F2 generation. It was also suggested that arsenic had transgenerational epigenetic effects, but more in-depth investigations are required to understand its underlying mechanistic underpinnings (Table 29.3).

29.7 Assessment of environmental arsenic exposure and effects on wildlife: Use of biomarkers

29.7.1 Biomarker

Biomarkers are defined as cellular and biochemical alterations in organism induced by exposure to a toxicant or xenobiotic. A wide array of biomarkers is often used to evaluate the level of exposure and effects of contaminants in exposed organisms. Generally, assessment of biomarkers in the wild or feral animals is performed in biological samples obtained mostly through noninvasive methods or by causing as little stress as possible to the targeted species. Most common biological samples used for measuring biomarkers of arsenic exposure to humans and in wildlife are hair, blood, nails, skin, and urine. Biomarkers are simple yet powerful indicators that can provide great insights into the exposure, susceptibility, and physiological effects of contaminants. Biomarkers help in the characterization and early detection of cellular and physiological effects and adverse structural or functional change in critical tissues and organs and can be useful in determining the susceptibility of the population for exposure to any specific contaminant.

29.7.2 Arsenic exposure and effects in wildlife near Giant Mine at Yellowknife, Canada (a case study)

Over the past few decades, mining for precious metals has increased many folds worldwide for various industrial and consumer applications. Because of the mining operation, the toxic elements that are otherwise buried beneath the surface of the earth are released into the biosphere through the discharge of mining waste and effluents. For example,

arsenic, copper, cadmium, chromium, nickel, and selenium are some of the toxic elements found in the mine tailings (the left-over part of the mineral ore after the extraction of the valuable metals). Over the years, there has been several documented cases of arsenic contamination in the environment in areas near gold and coal mines, leading to elevated exposure and adverse effects in both terrestrial and aquatic ecosystems [129]. In this section, we discussed the arsenic exposure and effects in wildlife living in the vicinity of the Giant Mine at Yellowknife, Canada, as a representative case study.

In early 1930s, gold deposits were first detected near the Yellowknife Bay of Great Bear Lake in Northwest Territories of Canada. The Giant Mine located in the city of Yellowknife became a major site of gold production from 1948 till its closure in 2004; however, the detrimental impacts of mining operation, particularly in terms of significant arsenic contamination in the surrounding environment, are evident till today and are likely to continue for decades. In Giant Mine, gold was produced by roasting of arsenopyrite ores, and in the process, approximately 20,000 tons of arsenic trioxide (AS_2O_3) was released into the surrounding environment. Moreover, 237,000 tons of AS_2O_3 were stored in underground chambers, which also become a significant source of arsenic in the surrounding environment due to leaching [130]. A vast amount of literature suggests that arsenic released from the Giant Mine has led to contamination of various compartments, such as soil, vegetation, and terrestrial and aquatic fauna. Fish and terrestrial mammals living in the Yellowknife area, which are often consumed by local indigenous communities, have also become a significant source for human exposure to arsenic [130–134].

Several studies reported arsenic levels in various tissues as biomarkers of arsenic exposure in local wildlife including fish and small mammals in and around the Yellowknife city. Markedly elevated levels of arsenic accumulation were observed in the liver and muscle in different fish species, such as lake whitefish (*Coregonus clupeaformis*), northern pike (*Esox lucius*), and burbot (*Lota lota*), collected from lakes in and around Yellowknife city. A significant proportion of accumulated arsenic in these fish species was found to exist as inorganic arsenic, which is more toxic than the organic forms of arsenic (Table 29.4). Recently refs [5, 6, 15, 16, 44, 135] reported arsenic levels in a variety of tissues (e.g., nail, bone, liver, kidney, and brain) and in the gut content in wild snowshoe hares (*Lepus americanus*), muskrats (*Ondatra zibethicus*), and red squirrels (*Tamiasciurus hudsonicus*) living in the Yellowknife area. These animals were considered suitable for pollution monitoring because of their small home range and diverse feeding habits (herbivore and omnivores). Animals were collected across three different sites to establish a gradient of arsenic exposure in local wildlife: site 1 (an area of 2 km radius from Giant Mine), site 2 ($\sim$20 km west of the Giant Mine), and site 3 ($\sim$100 km north-west of Giant Mine). Evidence from these studies suggested that small mammals living closest to the Giant mine were exposed to markedly elevated level of arsenic relative to their counterparts living in the area, which is farthest from the Giant Mine. For example, red squirrels and muskrats collected from site 1 had 5–50-fold greater arsenic in the gut content relative to their counterparts collected from site 3 [16]. In general, arsenic accumulation in various tissues in all three small mammal species examined also showed a consistent concentration gradient: site 1 $\geq$site 2 $>$ site 3 (Table 29.5). For example, arsenic accumulation in the nails of

Table 29.4 Accumulation of % inorganic arsenic (%iAs) in several fish species collected from lakes in and around Yellowknife.

Fish species	Location	%iAs ± standard deviation detected in muscle tissue
Northern pike	Lower Martin Lake	1.1 ± 0.5
Northern pike	Long Lake	1.7 ± 0.5
Lake whitefish	Grace Lake	3.2 ± 2.7
Northern pike	Kam Lake	3.7 ± 1.5
Northern pike	Yellowknife Bay	6.1 ± 3.7
Lake whitefish	Banting Lake	6.9 ± 3.6
Lake whitefish	Walsh Lake	7.7 ± 4.8
Lake whitefish	Yellowknife Bay	9.3 ± 6.7
Northern pike	Small Lake	10.4 ± 4.1
Northern pike	Great Slave Lake	14.1 ± 5.5
Lake whitefish	Lower Martin Lake	19.6 ± 14.9

Modified from Tanamal C, Blais JM, Yumvihoze E, Chan HM. Health risk assessment of inorganic arsenic exposure through fish consumption in Yellowknife, Northwest Territories, Canada. Human Ecol Risk Assess 2021;27:1072–93. https://doi.org/10.1080/10807039.2020.1799187.

Table 29.5 Range of arsenic concentrations (maximum-minimum; $\mu g\,g^{-1}$) in various tissues in different small mammals captured in and around Yellowknife, Northwest Territories, Canada.

Species	Site 1 (near Giant mine, 1–3 km)	Site 2 (20–30 km away from Giant mine)	Site 3 (50–100 km away from Giant mine; reference Site)	References
Snowshoe hare	**Nails:** 1.08–4.0 **Bones:** ND-0.026 **Stomach content:** 0.25–6.85 **Liver:** 0.19–2.30 **Kidney:** 0.334–4.0	Not studied	**Nails:** 0.047–0.936 **Bones:** ND **Stomach content:** 0.014–0.140 **Liver**: 0.015–0.766 **Kidney:** 0.023–0.945	[5]
Muskrat	**Nails**: 0.66–2.1 **Bone:** 0.20[a] **Stomach content:** 0.15–24.09 **Brain:** 0.06–4.18	**Nails:** <0.063–3.02 **Bone:** 0.21[a] **Stomach content**: 0.2–2.53 **Brian:** 0.072–0.95	**Nails:** <0.05–0.063 **Bone:** 0.13[a] **Stomach content:** 0.033–0.49 **Brain:** ND-0.063	[15,16,44,135]
Red Squirrel	**Nails:** ND-1.4 **Bone:** 0.16[a] **Stomach content:** 17.66[b]	**Nails:** ND-0.2 **Bone:** 0.12[a] **Stomach content:** 9.81[b]	**Nails:** ND **Bone:** 0.05[a] **Stomach content:** 0.44[b]	[15,16,44,135]

ND, nondetectable.

[a] Average.

[b] Maximum concentration.

muskrats and red squirrels from sites 1 and 2 were approximately 5–25 times higher than that in muskrats from site 3 [16]. Similarly, arsenic accumulation in liver, kidney, and brain was also approximately 3–5 times greater in these small mammals from site 1, relative to the animals from site 3 [5,6,15,16,135].

Although the environmental contamination of arsenic around Giant Mine raised a lot of public concerns about its impact on local wildlife for several decades, an in-depth investigation has never been carried out. Nonetheless, in a series of recent studies, refs. [5, 6, 15, 16, 44, 135] used a suite of biochemical and histopathological biomarkers to assess the health impacts of chronic arsenic exposure in snowshoe hares, muskrats, and red squirrels across three sites (site 1–3) as described above. The adverse effects were predominantly observed in animals captured in areas closer to the Giant Mine (sites 1 and 2), although the effects were not always consistent among the different species. A summary of various documented adverse effects in these three small species is provided in Table 29.6.

In general, animals living in site 1 were found to be suffering from oxidative stress as indicated by the altered of thiol status, lipid peroxidation and enzymatic antioxidant levels in target organs, which typically occurs in response to cellular ROS accumulation. For example, snowshoe hares from site 1 showed significant decrease in thiol redox and increase in lipid peroxidation in the liver relative to animals from site 3. In contrast, upregulation of enzymatic antioxidants (catalase, superoxide dismutase, and glutathione peroxidase) in the brain was recorded in muskrats and red squirrels from site 1, while the redox status and lipid peroxidation remained unaffected. Radiographic analysis of bones

Table 29.6 Major pathophysiological effects observed in different small mammals captured close to the Giant Mine (Site 1), Yellowknife, Northwest Territories, Canada.

Species	Documented pathophysiological effects	References
Snowshoe hare	• Extensive skeletal abnormalities, specifically abnormal bone growth, osteoporosis, cortical fractures, sclerosis, and cyst like changes in femur and vertebrae • Reduced biomechanical properties of the bone (stiffness, pick load) • Oxidative damage and fat accumulation in liver	[5,6]
Red squirrel	• Oxidative stress in the brain • Extensive shrinkage of core brain structures and brain cortex • Slightly elevated dopamine and serotonin levels in the brain • Severe skeletal abnormalities, such as loss of bone density and mass, and thinning of the femoral shafts with significant cystic lesions and bowing	[15,16,44,135]
Muskrat	• Severe ocular pathology, such as lymphocytic plasmacytic uveitis, inflammation of the cornea, subcapsular cataracts, and inner retinal degeneration • Oxidative stress in the brain • Decreased volume in specific brain regions, such as hippocampus, subcortical structures, amygdala, and somatosensory cortex and motor cortex • Severe bone deformities including extensive bone sclerosis and dysplasia, and osteocondensation	[15,16,44,135]

provided strong evidence of bone pathology, which included osteoporosis (decreased density of the bones), osteopenia (loss of bone mass), bone sclerosis (irregular calcification), and lesions. These osteological abnormalities are indicative of weaker bones, which are susceptible to fracture and were predominantly observed in all three species from site 1, although the effects were more prevalent in snowshoe hare and red squirrel. Histological analysis of the eye documented eye lesions, moderate-to-severe eye inflammation, reduction in the thickness of inner retina, and cataract in muskrats from site 1, although no such pathology in the eye was observed in snowshoe hare and red squirrel from the same location. Nonetheless, oxidative stress is known to cause structural and functional damage to mammalian eye [136], and thus the pathology of the eye documented in these studies was likely to be a consequence of chronic exposure to arsenic.

Moreover, arsenic is believed to cause neuro-behavioral impairments in animals via oxidative stress [73]. The magnetic resonance imaging analysis revealed pronounced neuroanatomical alterations in the brain of red squirrels and muskrats from site 1 including extensive shrinkage of cortex, striatum, thalamus, and hippocampal memory circuit of the forebrain [135]. The forebrain in mammals regulates a variety of critical functions including cognition, sensory, and voluntary motor functions, which are critical for the survival of these wild animals. Thus these brain pathologies reported in this study provided evidence of possible neurobehavioral dysfunctions in these animals because of chronic arsenic exposure.

Overall, this case study presented the real-world implications of chronic environmental exposure to arsenic in resident wildlife. The pathology of the vital organs, such as liver, bone, eye, and brain, documented here can decrease the scope of survival and reproductive fitness in impacted species eventually affecting their long-term sustenance of their population in the natural environment.

29.8 Environmental regulations of arsenic

The ecological risk assessment of many environmental contaminants including arsenic is generally performed using a qualitative approach where the information on the environmental concentration of a contaminant is compared against its no observed adverse effects level across different species to establish a benchmark value. If the concentration of a contaminant in any environmental compartment is found to be below the benchmark value, it poses no significant ecological risks. However, if the concentration of a contaminant exceeds the benchmark, it is usually classified as a contaminant of potential concern, which triggers further investigation. This approach is characterized as the first-tier approach and usually employed for environmental contaminants, such as arsenic for which established assessment criteria or guidelines (benchmark) values are available. The regulatory standards used ecological risk assessment of arsenic in the environment are often described as the criteria or guideline or trigger values depending on the jurisdiction, which are often derived using different methodologies that are beyond the scope of this chapter.

29.8.1 Regulatory standards for arsenic in freshwater and seawater

In many jurisdictions, different criteria or guideline values are applied to assess the ecological risks of arsenic contamination in freshwater and marine environments. Moreover, different criteria or guideline values have also been established for assessing the risk of acute and chronic toxicity from arsenic contamination in the aquatic environments. The current acute and chronic criteria values for freshwater and marine systems used in different jurisdictions are summarized in Table 29.7. These criteria or guidelines values are protective of most species in the resident environments, meaning that a significant risk of arsenic toxicity to resident species will only occur when the arsenic level in any freshwater or marine system will exceed the respective criteria value. For example, the freshwater and marine criteria for arsenic used by the United States Environmental Protection Agency are assumed to be protective of 95% of the freshwater and marine species, respectively. It is also important to note in most jurisdictions the criteria or guideline values for based on arsenic-III, which is the most toxic chemical form of arsenic.

29.8.2 Soil quality criteria

As described for aquatic systems, the regulatory standards for arsenic for protecting soil quality are defined differently depending on jurisdictions. In Denmark, China, and Sweden, it is referred as "soil quality criteria/standard," in the United States, it is called "soil screening levels (SSLs)," in Germany, it is defined as "target levels," in the United Kingdom, it is called "soil guideline values," and in Australia, it is characterized as "health-based or ecological investigation levels." In most jurisdictions, different soil environmental quality standards are developed with respect to residential, agricultural, commercial, and industrial sites, as presented in Table 29.8. These soil environmental quality standards are

Table 29.7 Arsenic criteria used for the protection of aquatic life in various jurisdictions.

Jurisdiction	Fresh water (acute) (μg/L)	Freshwater (chronic) (μg/L)	Saltwater (acute) (μg/L)	Saltwater (chronic) (μg/L)	References
United States	340 (total arsenic)	150 (total arsenic)	69 (total arsenic)	36 (total arsenic)	[137]
Australia/New	24 (Arsenic III)	NA	2.3 (Arsenic III)	NA	[138]
Zealand	13 (Arsenic V)	NA	4.5 (Arsenic V)	NA	
United Kingdom	8 (Arsenic III)	0.5 (Arsenic III)	1.1 (Arsenic III)	0.6 (Arsenic III)	[139]
South Africa	130 (Arsenic III)	20 (Arsenic III)	NA	12 (Arsenic III)	[140]
The Netherlands	NA	25 (Arsenic III)	NA	9.5 (Arsenic III)	[141]
Canada	NA	5 (Arsenic III)	NA	12.5 (Arsenic III)	[142]
China	167 (Arsenic III)	42 (Arsenic III)	384 (Arsenic V)	44 (Arsenic V)	[143]
India	NA	NA	19 (Arsenic III)	4.6 (Arsenic III)	[144]

NA, not available.

Table 29.8 Soil-environmental quality standards for arsenic in various jurisdictions.

		Land use			
Country/region	**Designation**	**Agricultural**	**Residential**	**Commercial**	**Industrial**
United States	Ecological-SSLs	18 (plants)	NA	NA	NA
Canada (Nunavut)	Soil quality guideline	12	12	12	12
Canada (Ontario)	Full-depth background site condition standard	11	18	18	18
United Kingdom	Soil guideline value	NA	20	500	500
Australia	Health-based investigation level	NA	100, 500, 300	3000	3000
	Ecological investigation level	NA	100	170	170
Germany	Trigger level (soil-human)	NA	50	140	140
Korea	Soil-contaminated protection level	6	6	20	20
	Soil contamination regulatory level	12	12	50	50

NA, not available.

All values are expressed as $mg\,kg^{-1}$.

Adapted from Zhou Q, Teng Y, Liu Y. A study on soil-environmental quality criteria and standards of arsenic. Appl Geochem 2017;77:158–66. https://doi.org/10.1016/J.APGEOCHEM.2016.05.001.

essentially designed to protect resident flora and fauna from arsenic toxicity and/or to conserve the capacity of soils to grow foods that are unlikely to cause toxic arsenic exposure to humans and thus protect human health.

29.9 Conclusion

Arsenic in the biosphere cannot be destroyed or eliminated, and it will continue to pose risks to human and ecological health until more effective strategies are developed to monitor arsenic exposure and effects in the environment. While the concentration of arsenic in potable water and food is regularly monitored in the interest of public health, the exposure of wildlife to arsenic is still largely ignored. Recent studies have demonstrated that chronic exposure to arsenic in contaminated systems can cause serious pathophysiological consequences for resident wildlife, some of which can be passed down to next generations threating their long-term sustenance. Therefore public awareness of the adverse ecological effects of arsenic is crucial. The lack of arsenic-specific biomarkers is a major impediment for the early detection of arsenic toxicity in wildlife; thus future research should employ cutting-edge molecular tools, such as transcriptomics, proteomics, or metabolomics, which may help in identifying reliable and sensitive predictive biomarkers of arsenic toxicity. Meanwhile, more useful alternate strategies of arsenic biomonitoring and ecological risk assessment should be developed. For example, invertebrates living in the soil and water usually occupy the lower trophic levels and play a critical role in the trophic transfer of arsenic up through the food webs. Thus biomonitoring of arsenic should focus on the

invertebrate community and can be useful in modeling arsenic exposure and effects in higher trophic level organisms. Current evidence also suggests that chronic low-level exposure to arsenic may not have any apparent effect on survival or reproductive fitness but still can induce subtle deleterious effects on neuro-endocrine functions and behavior in wildlife; however, these extremely sensitive endpoints are currently not taken into consideration in existing regulatory guidelines for arsenic in the environment. Furthermore, although the toxicity of inorganic forms of arsenic is well characterized, much less is known about the toxicity of organoarsenic metabolites. These organic forms of arsenic could also have genotoxic and epigenetic effects like their inorganic counterparts and should be investigated in future research. Overall, the biogeochemistry of arsenic is complex; thus a multi-tier approach is necessary to develop a more holistic understanding of the risks of arsenic contamination in the environment.

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