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A REVIEW OF ARSENIC HAZARDS TO PLANTS AND ANIMALS WITH EMPHASIS ON FISHERY AND WILDLIFE RESOURCES

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1. INTRODUCTION

Anxiety over arsenic (As) is understandable and frequently justifiable. Arsenic compounds were the preferred homicidal and suicidal agents during the Middle Ages, and arsenicals have been regarded largely in terms of their poisonous characteristics in the nonscientific literature [National Academy of Sciences (NAS), 1977]. Data collected on animals, including human beings, indicate that inorganic arsenic can cross the placenta and produce mutagenic, teratogenic, and carcinogenic effects in offspring (Nagymajtenyi et al., 198.5). Correlations between elevated atmospheric arsenic levels and mortalities from cancer, bronchitis, and pneumonia were established in an epidemiological study in England and Wales, where deaths from respiratory cancer increased at air concentrations $> 3\mu g$ As/m^3 [National Research Council of Canada (NRCC), 1978]. Chronic arsenical poisoning, including skin cancer and a gangrenous condition of the hands and feet called blackfoot disease, has occurred in people from communities in Europe, South America, and Taiwan who were exposed to elevated concentrations of arsenic in drinking water [Environmental Protection Agency (EPA), 1980]. More recently, about 12,000 Japanese infants were poisoned (128 deaths) after consuming dry milk containing 15 to 24 mg inorganic As/kg, which originated from contaminated sodium phosphate used as a milk stabilizer. Fifteen years after exposure, the survivors sustained an elevated frequency of severe hearing loss and brain-wave abnormalities (Pershagen and Vahter, 1979).

Many reviews on the ecotoxicological aspects of arsenic in the environment are available; particularly useful are those by Woolson (1975), NAS (1977), NRCC (1978), Pershagen and Vahter (1979), EPA (1980, 1985), Hood (1985), Andreae (1986), Eisler (1988), and Phillips (1990). These authorities agree on six points: (1) arsenic is a relatively common element and is present in air, water, soil, plants, and all living tissues; (2) arsenicals have been used in medicine as chemotherapeutics since 400 B.C.E., and organoarsenicals were used extensively for this purpose until about 1945, with no serious effects when judiciously administered; (3) large quantities of arsenicals are released into the environment as a result of industrial and especially agricultural activities, and these may pose potent ecological dangers; (4) exposure of humans and wildlife to arsenic may occur through air (emissions from smelters, coal-fired power plants, herbicide sprays), water (mine tailings runoff, smelter wastes, natural mineralization), and food (especially seafoods); (5) chronic exposure to arsenicals by way of the air, diet, and other routes is associated with liver, kidney, and heart damage, hearing loss, brain-wave abnormalities, and impaired resistance to viral infections; and (6) exposure to arsenic has been associated with different types of human cancers,

such as respiratory cancers and epidermoid carcinomas of the skin, as well as precancerous dermal keratosis. Only recently (Deknudt et al., 1986) has the epidemiological evidence of human carcinogenicity been confirmed by carcinogenesis in experimental animals.

This account briefly reviews the ecological and toxicological aspects of arsenic in the environment, with emphasis on fish, wildlife, and invertebrates, and updates my earlier report (Eisler, 1988) on this subject.

2. SOURCES, FATE, AND USES

Global production of arsenic is estimated to be 75,000 to 100,000 tons annually, of which the United States produces about 21,000 tons and uses about 44,000 tons; major quantities are imported from Sweden, the world's leading producer (NAS, 1977; EPA, 1980). Almost all (97%) of the arsenic made worldwide enters end-product manufacture in the form of arsenic trioxide (As_2O_3), and the rest is used as additives in producing special lead and copper alloys (NAS, 1977). More than 80% of the As_2O_3 is used to manufacture products with agricultural applications, such as insecticides, herbicides, fungicides, algicides, sheep dips, wood preservatives, dyestuffs, and medicines for the eradication of tapeworm in sheep and cattle (NAS, 1977). The sole producer and refiner of As_2O_3 in the United States is a copper smelter in Tacoma, Washington (NAS, 1977).

Arsenic occurs naturally as sulfides and as complex sulfides of iron, nickel, and cobalt (Woolson, 1975). In one form or another, arsenic is present in rocks, soils, water, and living organisms at concentrations of parts per billion to parts per million (NAS, 1977). Soil arsenic levels are normally elevated near arseniferous deposits and in mineralized zones containing gold, silver, and sulfides of lead and zinc (Dudas, 1984). Secondary iron oxides formed from the weathering of pyrite act as scavengers of arsenic (Dudas, 1984). Pyrite is a known carrier of arsenic and may contain up to 5600 mg/kg; for example, total arsenic is 10 times above normal background levels in soils derived from pyritic shale (Dudas, 1984). Natural weathering of rocks and soils adds about 40,000 tons of arsenic to the oceans yearly, accounting for < 0.01 mg/L input to water on a global basis (NRCC, 1978). Many species of marine plants and animals often contain naturally high concentrations of arsenic (NAS. 1977), but it is usually present in a harmless organic form (Woolson, 1975). Anthropogenic input of arsenic to the environment is substantial and exceeds the amount contributed by natural weathering processes by a factor of about three (NRCC, 1978).

The most important factor in arsenic cycling in the environment is constant change. Arsenic is ubiquitous in living tissue and is constantly being oxidized, reduced, or otherwise metabolized. In soils, insoluble or slightly soluble arsenic compounds are constantly being resolubilized, and the arsenic is being presented for plant uptake or reduction by organisms and chemical processes. Human beings reportedly have modified the arsenic cycle only by causing localized high concentrations (NAS, 1977). The speciation of arsenic in the environment is

affected partly by indiscriminate biological uptake, which consumes about 20% of the dissolved arsenate pool and results in measurable concentrations of reduced and methylated arsenic species. The overall arsenic cycle is similar to the phosphate cycle; however, regeneration time for arsenic is much slower-on the order of several months (Sanders, 1980). The ubiquity of arsenic in the environment is evidence of the redistribution processes that have been operating since early geologic time (Woolson, 1975). The prehuman steady-state global arsenic cycle (Austin and Millward, 1984) indicates that major reservoirs of arsenic (in kilotons) are magma (50 billion), sediments (25 billion), oceanic deep waters (1.56 million), land (1.4 million), and ocean mixed layers (270,000); minor amounts occur in ocean particulates (100) and in continental (2.5) and marine tropospheres (0.069). Arsenic is significantly mobilized from the land to the troposphere by natural and anthropogenic processes. Industrial emissions account for about 30% of the present-day burden of arsenic in the troposphere (Austin and Millward, 1984). Agronomic ecosystems, for example, may receive arsenic from agricultural sources such as organic herbicides, irrigation waters, and fertilizers, and from nonagricultural sources such as fossil fuels and industrial and municipal wastes (Woolson, 1975). Arsenic is mobile and nonaccumulative in the air, plant, and water phases of agronomic ecosystems; arsenicals sometimes accumulate in soils, but redistribution mechanisms usually preclude hazardous accumulations (Woolson, 1975).

Arsenic compounds have been used in medicine since the time of Hippocrates, ca. 400 B.C.E. (Woolson, 1975). Inorganic arsenicals have been used for centuries, and organoarsenicals have been used for at least a century in the treatment of syphylis, yaws, amoebic dysentery, and trypanosomiasis (NAS, 1977). During the period 1200 to 1650, arsenic was used extensively in homicides (NRCC, 1978). In 1815, the first accidental death was reported from arsine (AsH_3) poisoning, and in 1900 to 1903 accidental poisonings from consumption of arsenic-contaminated beer were widely reported (NRCC, 1978). In 1938, arsenic was found to counteract selenium toxicity (NRCC, 1978). The introduction of arsphenamine, an organoarsenical, to control venereal disease earlier in this century gave rise to intensive research by organic chemists, which resulted in the synthesis of at least 32,000 arsenic compounds. The advent of penicillin and other newer drugs, however, nearly eliminated the use of organic arsenicals as human therapeutic agents (EPA, 1980). Arsenical drugs are still used in treating certain tropical diseases, such as African sleeping sickness and amoebic dysentery, and in veterinary medicine to treat parasitic diseases, including filariasis in dog (*Canis familiaris*) and blackhead in turkeys (*Meleagris gallopavo*) and chickens (Callus spp.) (NAS, 1977). Today, abnormal sources of arsenic that can enter the food chain from plants or animals include arsenical pesticides such as lead arsenate; arsenic acid, $HAsO_3$; sodium arsenite, $NaAsO_2$; sodium arsenate, Na_2AsO_4; and cacodylic acid, $(CH_3)_2As(OH)$ (NAS, 1977).

The major uses of arsenic are in the production of herbicides, insecticides, desiccants, wood preservatives, and growth stimulants for plants and animals. Much smaller amounts are used in the manufacture of glass (nearly all of which

contains 0.2 to 1 .0% arsenic as an additive-primarily as a decolorizing agent) and textiles, and in medical and veterinary applications **(NAS, 1977; EPA, 1980).** Arsenic is also an ingredient in lewisite, a blistering poison gas developed (but not used) during World War I, and in various police riot-control agents (NAS, 1977). The availability of arsenic in certain local areas has been increased by various human activities: smelting and refining of gold, silver, copper, zinc, uranium, and lead ores; combustion of fossil fuels, such as coal and gasoline; burning of vegetation from cotton gins treated with arsenical pesticides; careless or extensive use of arsenical herbicides, pesticides, and defoliants; dumping of land wastes and sewage sludge (1.1 mg As/L) in areas that allow leaching into groundwater; use of domestic detergents in wash water (2.5 to 1000 mg As/L); manufacture of glass; and the sinking of drinking-water wells into naturally arseniferous rock (NRCC, 1978; EPA, 1980). There are several major anthropogenic sources of environmental arsenic contamination: industrial smelters-the effluent from a copper smelter in Tacoma, Washington, contained up to 70 tons of arsenic discharged yearly into nearby Puget Sound (NRCC, 1978); coal-fired power plants, which collectively emit about 3000 tons of arsenic annually in the United States (EPA, 1980); and the production and use of arsenical pesticides, coupled with careless disposal of used pesticide containers (NAS, 1977). Elevated levels of arsenic have been reported in soils near smelters, in acid mine spoils, and in orchards receiving heavy applications of lead arsenate (NAS, 1977; Dudas, 1984). Air concentrations of arsenic are elevated near metal smelters, near sources of coal burning, and wherever arsenical pesticides are applied (NAS, 1977). Atmospheric deposition of arsenic has steadily increased for at least 30 years, on the basis of sedimentary evidence from lakes in upstate New York (Smith et al., 1987). Arsenic is introduced into the aquatic environment through atmospheric deposition of combustion products and through runoff from fly ash-storage areas near power plants and nonferrous smelters (Smith et al., 1987). Elevated arsenic concentrations in water were recorded near mining operations, and from mineral springs and other natural waters-usually alkaline with high sodium and bicarbonate contents (NAS, 1977). In the United States, the most widespread and frequent increases in dissolved arsenic concentrations in river waters have been in the northern Midwest; all evidence indicates that increased atmospheric deposition of fossil-fuel combustion products is the predominant cause of the trend (Smith et al., 1987).

Agricultural applications are the largest anthropogenic sources of arsenic in the environment (Woolson, 1975). Inorganic arsenicals (arsenic trioxide; arsenic acid; arsenates of calcium, copper, lead, and sodium; and arsenites of sodium and potassium) have been used widely for centuries as insecticides, herbicides, algicides, and desiccants. Paris green (cuprous arsenite) was successfully used in 1867 to control the Colorado potato beetle (*Leptinotarsa decemlineata*) in the eastern United States. Arsenic trioxide has been applied widely as a soil sterilant. Sodium arsenite has been used for aquatic weed control, as a defoliant to kill potato vines before tuber harvest, as a weed killer along roadsides and railroad rights-of-way, and for control of crabgrass (*Digitaria sanguinalis*). Calcium arsenates have been applied to cotton and tobacco fields to protect against the

boll weevil *(Anthonomus grandis)* and other insects. Lead arsenate has been used to control insect pests on fruit trees, and for many years it was the only insecticide that controlled the codling moth (*Carpocapsa pomonella*) in apple orchards and the horn worm larva (Sphyngidae) on tobacco. Much smaller quantities of lead arsenate are used in orchards now that fruit growers rely primarily on carbamate and organophosphorus compounds to control insect pests; however, lead arsenate is still being used by some growers to protect orchards from certain chewing insects. The use of inorganic arsenicals has decreased in recent years due to the banning of sodium arsenite and some other arsenicals for most purposes, although they continue to be used on golf greens and fairways in certain areas to control annual bluegrass *(Pou* unnuu). In recent decades, inorganic arsenicals have been replaced by organoarsenicals for herbicidal application, and by carbamate and organophosphorus compounds for insect control (Woolson, 1975). By the mid-1950s, organoarsenicals were used extensively as desiccants, defoliants, and herbicides (NRCC, 1978). Organoarsenicals marketed in agriculture today, and used primarily for herbicidal application, include cacodylic acid (also known as dimethylarsinic acid) and its salts, monosodium and disodium methanearsonate (Woolson, 1975; NAS, 1977). Organoarsenicals are used as selective herbicides for weedy grasses in turf, and around cotton and noncrop areas for weed control; at least 1.8 million ha (4.4 million acres) have been treated with more than 8000 tons of organoarsenicals (NAS, 1977). In 1945, one organoarsenical (3-nitro-4-hydroxyphenylarsonic acid) was found to control coccidiosis and promote growth in domestic chickens (Woolson, 1975). Since that time, other substituted phenylarsonic acids have been shown to have both therapeutic and growth-promoting properties as feed additives for poultry and swine (*Sus* spp.), and they are used for this purpose today under existing regulations (Woolson, 1975; NAS, 1977), although the use of arsenicals in poultry food was banned in France in 1959 (NRCC, 1978).

3. CHEMICAL AND BIOCHEMICAL PROPERTIES

Elemental arsenic is a gray, crystalline material. Its atomic number is 33, its atomic weight is 74.92, its density is 5.727, its melting point is 817 °C, and its sublimation point is 613 °C; its chemical properties are similar to those of phosphorus (Woolson, 1975; NAS, 1977; NRCC, 1978; EPA, 1980, 1985). Arsenic has four valence states: $-3, 0, +3$, and $+5$. Arsines and methylarsines, which are characteristic of arsenic in the -3 oxidation state, are generally unstable in air. Elemental arsenic (As^0) is formed by the reduction of arsenic oxides. Arsenic trioxide (As^{+3}) is a product of smelting operations and is the material used in synthesizing most arsenicals. It is oxidized catalytically or by bacteria to arsenic pentoxide (As^{+5}) or orthoarsenic acid (H_3AsO_4). Arsenic in nature is rarely in its free state. Usually, it is a component of sulfidic ores, occurring as arsenides and arsenates, along with arsenic trioxide, which is a weathering product of arsenides. Most arsenicals degrade or weather to form arsenate, although arsenite may form

under anaerobic conditions. Biotransformations may occur, resulting in volatile arsenicals that normally are returned to the land, where soil adsorption, plant uptake, erosion, leaching, reduction to arsines, and other processes occur. This natural arsenic cycle entails a constant shifting of arsenic between environmental compartments.

Arsenic species in flooded soils and water are subject to chemically and microbiologically mediated oxidation or reduction and methylation reactions. At high Eh values (i.e., high oxidation-reduction potential) typical of those encountered in oxygenated waters, pentavalent As^{+5} tends to exist as H_3AsO_4, $H_2AsO_4^-$, $HAsO_2$, and AsO_4^{3-}. At lower Eh, the corresponding trivalent arsenic species can be present, as well as AsS_2^- (Thanabalasingam and Pickering, 1986). In aerobic soils, the dominant arsenic species is As^{+5}, and small quantities of arsenite and monomethylarsonic acid are present in mineralized areas; in anaerobic soils, As^{+3} is the major soluble species (Haswell et al., 1985). Inorganic arsenic is more mobile than organic arsenic and thus poses greater problems by leaching into surface waters and groundwater (NRCC, 1978). The trivalent arsenic species are generally considered to be more toxic, more soluble, and more mobile than As^{+5} species (Thanabalasingam and Pickering, 1986). Soil microorganisms metabolize arsenic into volatile arsine derivatives. Depending on conditions, 17 to 60% of the total arsenic present in soil may be volatilized (NRCC, 1978). Estimates of the half-life of arsenic in soil vary from 6.5 years for arsenic trioxide to 16 years for lead arsenate (NRCC, 1978).

In water, arsenic occurs in both inorganic and organic forms and in dissolved and gaseous states (EPA, 1980). The form of arsenic in water depends on Eh, pH, organic content, suspended solids, dissolved oxygen, and other variables (EPA, 1985). Arsenic in water exists primarily as a dissolved ionic species; particulates account for $< 1\%$ of the total measurable arsenic (Maher, 1985a). Arsenic is rarely found in water in the elemental state (0), and it is found in the -3 state only at extremely low Eh values (Lima et al., 1984). Common forms of arsenic encountered in water are arsenate, arsenite, methanearsonic acid, and dimethylarsinic acid (EPA, 1985). The formation of inorganic pentavalent arsenic, the most common species in water, is favored under conditions of high dissolved oxygen, basic pH, high Eh, and reduced organic material content; the opposite conditions usually favor the formation of arsenites and arsenic sulfides (NRCC, 1978; Pershagen and Vahter, 1979; EPA, 1980), although some arsenite is attributed to biological activity (Maher, 1985a). Water temperature seems to affect arsenic species composition in the estuary of the River Beaulieu in the United Kingdom, where reduced and methylated species predominate during the warmer months and inorganic As^{+5} predominates during the colder months; the appearance of methylated arsenicals during the warmer months is attributed to bacterial and abiotic release from decaying plankton and to grazing by zooplankton (Howard et al., 1984). Also contributing to higher water or mobile levels are the natural levels ofpolyvalent anions, especially phosphate species. Phosphate, for example, displaces arsenic held by humic acids, and it sorbs strongly on the hydrous oxides of arsenates (Thanabalasingam and Pickering, 1986).

Physical processes play a key role in governing arsenic bioavailability in aquatic environments. For example, arsenates are readily sorbed by colloidal humic material under conditions of high organic content, low pH, low phosphate, and low mineral content (EPA, 1980; Thanabalasingam and Pickering, 1986). Arsenates also coprecipitate with. or adsorb on, hydrous iron oxides and form insoluble precipitates with calcium, sulfur, aluminium, and barium compounds (EPA, 1980). Removal of arsenic from seawater by iron hydroxide scavenging seems to be the predominant factor in certain estuaries. The process involves both As^{+3} and As' ^{5} and results in a measurable increase in arsenic level of particulate matter, especially at low salinities (Sloot et al., 1985; Tremblay and Gobeil, 1990). Arsenic sulfides are comparatively insoluble under conditions prevalent in anaerobic aqueous and sedimentary media containing hydrogen sulfide; accordingly, these compounds may accumulate as precipitates and thus remove arsenic from the aqueous environment. In the absence of hydrogen sulfide, these sulfides decompose within several days to form arsenic oxides, sulfur, and hydrogen sulfide (NAS, 1977).

In reduced environments such as sediments, arsenate is reduced to arsenite and methylated to methylarsinic acid or dimethylarsenic acids. These compounds may be further methylated to trimethylarsine or reduced to dimethylarsine, and they may volatilize to the atmosphere, where oxidation reactions result in the formation of dimethylarsinic acid (Woolson, 1975). Arsenates are more strongly adsorbed to sediments than are other arsenic forms, the adsorption processes depending strongly on arsenic concentrations, sediment characteristics, pH, and ionic concentration of other compounds (EPA, 1980). An important mechanism of arsenic adsorption onto lake sediments involves the interaction of anionic arsenates and hydrous iron oxides. Evidence indicates that arsenic is incorporated into sediments at the time of hydrous oxide formation, rather than by adsorption onto existing surfaces (Aggett and Roberts, 1986). Arsenic concentrations in lake sediments are also correlated with manganese; hydrous manganese oxides-positively charged for the adsorption of Mn^{+2} ions- play a significant role in arsenic adsorption onto the surface of lake sediments (Takamatsu et al., 1985). The mobility of arsenic in lake sediments and its release to the overlying water is related partly to seasonal changes. In areas that become stratified in summer, arsenic released from sediments accumulates in the hypolimnion until turnover, when it is mixed with epilimnetic waters; this mixing may result in a 10 to 20% increase in arsenic concentration (Aggett and O'Brien, 1985). Microorganisms (including four species of fungi) in lake sediments oxidized inorganic As^{+3} to As^{+5} and reduced inorganic As^{+5} to As^{+3} under aerobic conditions; under anaerobic conditions, only reduction was observed (Freeman et al., 1986). Inorganic arsenic can be converted to organic alkyl arsenic acids and methylated arsines under anaerobic conditions by fungi, yeasts, and bacteria, although biomethylation may also occur under aerobic conditions (EPA, 1980).

Most arsenic investigators now agree on the following points: (1) arsenic may be absorbed by ingestion, inhalation, or through permeation of the skin or mucous membranes; (2) cells accumulate arsenic by using an active transport

system normally used in phosphate transport; (3) arsenicals are readily absorbed after ingestion, most being rapidly excreted in the urine during the first few days, or at most a week (the effects seen after long-term exposure are probably a result of continuous daily exposure rather than accumulation); (4) the toxicity of arsenicals conforms to the following order, from greatest to least toxicity: arsines > inorganic arsenites > organic trivalent compounds (arsenoxides) > inorganic arsenates > organic pentavalent compounds > arsonium compounds > elemental arsenic; (5) solubility in water and body fluids appears to be directly related to toxicity (the low toxicity of elemental arsenic is attributed to its virtual insolubility in water and body fluids, whereas the highly toxic arsenic trioxide, for example, is soluble in water to 12.0 g/L at 0 °C, 2 1 .O g/L at 25 °C, and 56.0 g/L at 75 "C); and (6) the mechanisms of arsenical toxicity differ considerably among arsenic species, although signs of poisoning appear to be similar for all arsenicals (Woolson, 1975; NRCC, 1978; Pershagen and Vshter, 1979).

The primary toxicity mode of inorganic As^{+3} is through reaction with sulfhydryl groups of proteins and subsequent enzyme inhibition; inorganic pentavalent arsenate does not react as readily as As^{+3} with sulfhydryl groups, but may uncouple oxidative phosphorylation (Howard et al., 1984; EPA, 1985). Inorganic As^{+3} interrupts oxidative metabolic pathways and sometimes causes morphological changes in liver mitochondria. Arsenite in vitro reacts with protein-SH groups to inactivate enzymes such as dihydrolipoyl dehydrogenase and thiolase, producing inhibited oxidation of pyruvate and beta-oxidation of fatty acids (Belton et al., 1985). Inorganic As^{+3} may also exert toxic effects by the reaction of arsenous acid (HAsO) with the sulfhydryl (SH) groups of enzymes. In the first reaction, arsenous acid is reduced to arsonous acid ($AsOH_2$), which then condenses to either monothiols or dithiols to yield dithioesters of arsonous acid. Arsonous acid may then condense with enzyme-SH groups to form a binary complex (Knowles and Benson, 1984a, b).

Methylation to methylarsonic acid $[(CH_3)_2AsO_3H_2]$ and dimethylarsinic acid $[(CH_3)_2AsO_2H]$ is usually the major detoxification mechanism for inorganic pentavalent arsenates and trivalent arsenites in mammals. Methylated arsenicals rapidly clear from all tissues, except perhaps the thyroid (Marafante et al., 1985; Vahter and Marafante, 1985; Yamauchi et al., 1986). Methylated arsenicals are probably common in nature. Methylation of arsenic (unlike methylation of mercury) greatly reduces toxicity and is a true detoxification process (Woolson, 1975). Before methylation (which occurs largely in the liver), As^{+5} is reduced to As^{+3} the kidney being an important site for this transformation (Belton et al., 1985). Arsenate reduction and subsequent methylation is rapid. Arsenite and dimethylarsinate were present in hamster (*Cricetus* sp.) plasma only 12 minutes after injection of inorganic As^{+5} (Hanlon and Ferm, 1986c). Demethylation of methylated arsenicals formed in vivo has not yet been reported (EPA, 1980).

The toxic effects of organoarsenicals are exerted by initial metabolism to the trivalent arsonoxide form, and then by reaction with sulfhydryl groups of tissue proteins and enzymes to form an arylbis (organylthio) arsine (NAS, 1977). This

form, in turn, inhibits oxidative degradation of carbohydrates and decreases cellular ATP, the energy-storage molecule of the cell (NRCC, 1978). Among the organoarsenicals, those most injurious physiologically are methylarsonous acid [$CH_3As(OH)_2$] and dimethylarsinous acid [$(CH_3)_2AsOH$] (Knowles and Benson, 1984b). The enzyme inhibitory forms of organoarsenicals (arsonous acid) are formed from arsenous acid, and the corresponding arsonic acids are formed by a wide variety of enzymes and subcellular particles (Knowles and Benson, 1984a). Organoarsenicals used as growth promoters and drugs are converted to more easily excretable (and sometimes more toxic) substances, although most organoarsenicals are eliminated without being converted to inorganic arsenic or to demethylarsinic acids (Pershagen and Vahter, 1979).

4. ESSENTIALITY, SYNERGISM, AND ANTAGONISM

Arsenic apparently behaves more like an environmental contaminant than a nutritionally essential mineral (NAS, 1977). Nevertheless, low doses (< 2 μg/day) of arsenic stimulated growth and metamorphosis in tadpoles and increased viability and cocoon yield in silkworm caterpillars (NAS, 1977). Arsenic deficiency has been observed in rats: signs include rough haircoat, low growth rate, decreased hematocrit, increased fragility of red cells, and enlarged spleen (NAS, 1977). Similar results have been documented in goats and pigs fed diets containing less than 0.05 mg As/kg. In these animals, reproductive performance was impaired, neonatal mortality was increased, birth weight was lower, and weight gain in second-generation animals was decreased; these effects were not evident in animals fed diets containing 0.35 mg As/kg (NAS, 1977).

The use of phenylarsonic feed additives to promote growth in poultry and swine and to treat specific diseases does not seem to constitute a hazard to the animal or its consumers. Animal deaths and elevated tissue arsenic residues occur only when the arsenicals are fed at excessive dosages for long periods (NAS, 1977). Arsenic can be detected at low levels in tissues of animals fed organoarsenicals, but it is rapidly eliminated when the arsenicals are removed from the feed for the required 5-day period before marketing (Woolson, 1975).

Selenium and arsenic are antagonists in several animal species. In rats, dogs, swine, cattle, and poultry, the arsenic protects against selenium poisoning if arsenic is administered in the drinking water and selenium in the diet (NAS, 1977; NRCC, 1978; Pershagen and Vahter, 1979). Inorganic arsenic compounds decrease the toxicity of inorganic selenium compounds by increasing biliary excretion (NRCC, 1978). However, in contrast to the antagonism shown by inorganic arsenic-inorganic selenium mixtures, the toxic effects of naturally methylated selenium compounds (trimethylselenomium chloride and dimethyl selenide) are markedly enhanced by inorganic arsenicals (NRCC, 1978).

The toxic effects of arsenic can be counteracted with (1) saline purgatives, (2) various demulcents that coat irritated gastrointestinal mucous membranes, (3) sodium thiosulfate (NAS, 1977), and (4) mono- and dithiol-containing com-

pounds and 2,3-dimercaptopropanol (Pershagen and Vahter, 1979). Arsenic uptake in rabbit intestine is inhibited by phosphate, casein, and various metal chelating agents (EPA, 1980). Mice and rabbits are significantly protected against sodium arsenite intoxication by *N*-(2,3-dimercaptopropyl) phthalamidic acid (Stine et al., 1984). Conversely, the toxic effects of arsenite are potentiated by excess dithiols, cadmium, and lead, as evidenced by reduced food efficiency and disrupted blood chemistry in rodents (Pershagen and Vahter, 1979).

Arsenic effectively controls filariasis in cattle; new protective uses are under investigation. The control of parasitic nematodes (*Parafilaria bovicola*) in cattle was successful after 30 weekly treatments in plungement dips containing 1600 mg As_2O_3/L; however, the muscle of treated cattle contained up to 1.3 mg As/kg, or 12 times the amount in controls (Nevill, 1985). Existing anionic organic arsenicals used to control tropical nematode infections in humans have sporadic and lethal side effects. Cationic derivatives have been synthesized in an attempt to avoid the side effects and have been examined for their effect on adult nematodes (*Brugia* pahangi) in gerbils (*Meriones unguiculatus*). All arsenicals were potent filaricides; the most effective compounds tested killed 95% of adult *B. pahangi* after five daily subcutaneous injections of 3.1 mg As/kg body weight (Denham et al., 1986).

Animals previously exposed to sublethal levels of arsenic may develop tolerance to arsenic on reexposure. Although the mechanism of this process is not fully understood, it probably includes the efficiency of in vivo methylation processes (EPA, 1980). For example, resistance to toxic doses of As^{+3} or As^{+5} increases in mouse fibroblast cells pretreated with a low As^{+3} concentration (Fischer et al., 1985). Also, growth is better in arsenic-conditioned mouse cells in the presence of arsenic than in previously unexposed cells, and inorganic arsenic is more efficiently methylated. In vivo biotransformation and excretion of inorganic arsenic as monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA) have been demonstrated in a number of mammalian species, including human beings. Cells may adapt to arsenic by increasing the biotransformation rate of the element to methylated forms, such as MMA and DMA (Fischer et al., 1985). Pretreatment of Chinese hamster (*Cricetus* spp.) ovary cells with sodium arsenite provided partial protection against the adverse effects of methyl methanesulfonate (MMS), and may even have benefited the MMS-treated cells; however, posttreatment dramatically increased the cytotoxic, clastogenic, and mitotic effects of MMS (Lee et al., 1986b).

Although arsenic is not an essential plant nutrient, small yield increases have sometimes been observed at low soil-arsenic levels, especially for tolerant crops such as potatoes, corn, rye, and wheat (Woolson, 1975). Arsenic phytotoxicity of soils is reduced with increasing lime, organic matter, iron, zinc, and phosphates (NRCC, 1978). In most soil systems, the chemistry of arsenic becomes the chemistry of arsenate; the estimated half-time of arsenic in soils is about 6.5 years, although losses of 60% in 3 years and 67% in 7 years have been reported (Woolson, 1975). Additional research is warranted on the role of arsenic in crop production and nutrition, with special reference to essentiality for aquatic and terrestrial wildlife.

5. BACKGROUND CONCENTRATIONS

In abundance, arsenic ranks twentieth among the elements in the earth's crust (1.5 to 2 mg/kg), fourteenth in seawater, and twelfth in the human body (Woolson, 1975). It occurs in various forms, including inorganic and organic compounds and trivalent and pentavalent states (Pershagen and Vahter, 1979). In aquatic environments, higher arsenic concentrations are reported in hot springs, in groundwaters from areas of thermal activity or in areas containing rocks with high arsenic content, and in some waters with high dissolved-salt content (NAS, 1977). Most of the other elevated values reported in lakes, rivers, and sediments are probably due to anthropogenic sources, which include smelting and mining operations, combustion of fossil fuels, arsenical grasshopper baits, synthetic detergent and sewage sludge wastes, and arsenical defoliants, herbicides, and pesticides (NAS, 1977). Most living organisms normally contain measurable concentrations of arsenic, but except for marine biota, these are usually less than 1 mg/kg fresh weight. Marine organisms, especially crustaceans, may contain more than 100 mg As/kg dry weight, usually as arsenobetaine, a water-soluble organoarsenical that poses little risk to the organism or its consumer. Plants and animals collected from naturally arseniferous areas or near anthropogenic sources may contain significantly elevated tissue residues of arsenic. Additional and more detailed information on background concentrations of arsenic in abiotic and living resources can be found in NAS (1977), Hall et al. (1978), NRCC (1978), EPA (1980), Jenkins (1980), Eisler (1981), and Phillips (1990).

5.1. Nonbiological Samples

Arsenic is a major constituent of at least 245 mineral species, of which arsenopyrite is the most common (NAS, 1977). In general, background concentrations of arsenic are 0.2 to 15 mg/kg in the lithosphere, 0.005 to 0.1 $\mu g/m^3$ in air, < 10 $\mu g/l$ in water, and < 1.5 mg/kg in soil (NRCC, 1978). Commercial use and production of arsenic compounds have raised local concentrations in the environment far above natural background concentrations (Table 1).

Weathering of rocks and soils adds about 45,000 tons of arsenic to the oceans annually, accounting for < 0.01 mg/L on a global basis (NRCC, 1978). However, arsenic inputs to oceans increased during the past century from natural sources and as a result of industrial use, agricultural and deforestation activities, emissions from coal and oil combustion, and loss during mining of metal ores. If present activities continue, arsenic concentrations in oceanic surface waters may increase overall by about 2% by the year 2000; most of the increased burden will be in estuaries and coastal oceans, for example, Puget Sound, Washington; the Tamar, England; and the Tejo, Portugal (Sanders, 1985). Estimates of residence times of arsenic are 60,000 years in oceans and 45 years in freshwater lakes (NRCC, 1978). In the hydrosphere, inorganic arsenic occurs predominantly as As^{+5} in surface water, and significantly as As^{+3} in groundwater containing high levels of total arsenic. The main organic species in freshwater are methylarsonic

Table I Total Arsenic Concentrations in Selected Nonbiological Materials

Material (concentration unit)	Concentration [mean, (range), max.]	Reference"
AIR ($\mu g/m^3$)		
Remote areas	< 0.02 1	1
Urban areas	(0.0-O. 16)	1
Near smelters		
Former USSR	(0.5–1.9)	2
Texas	Max. 1.4	2
Tacoma, Washington	Max. 1.5	2
Romania	Max. 1.6	2
Germany	(0.9–1.5)	2
Coal-fired power plant, Czechoslovakia	(19-69)	3
Orchard spraying of Pb arsenate	Max. 260.000	3
Near U.S. cotton gin burning vegetation treated with arsenic	Max. 400	3
DRINKING WATER ($\mu g/L$)		
Nationwide, USA	2.4 (0.5-214)	4
Fairbanks, Alaska	224 (1-2450)	4
Bakersfield, California	(6-393)	4
Nevada, 3 communities	(51-123)	4
Mexico, from plant producing As_2O_3	(4000–6000)	2
Japan, near factory producing arsenic sulfide	3000	2
Ghana, near gold mine	1400	2
Minnesota, contaminated by residual arsenical grasshopper bait	(11,800–21,000)	1
Methylated arsenicals, USA	Usually < 0.3 (0.01 – 1)	5
DUST (mg/kg)		
Tacoma, Washington		
Near smelter	1300	1
Remote from smelter	70	1
FOSSIL FUELS (mg/kg)		
Coal		
Canada	4 (0.3–100)	3
USA	5	2
Czechoslovakia	Max. 1500	2
Worldwide	13 (0.0-2000)	I
Coal ash	(< 20-8000)	3
Fly ash	(2.88200)	3
Petroleum	0.2 (2.88200)	3
Petroleum ash	Max. 100,000	3
Automobile particulates	298	3
GROUNDWATER ($\mu g/L$)		
Near polymetallic sulfide deposits	Max. 400,000	3
Near gold mining activities	> 50	3

Table 1 *(Continued)*

Material (concentration unit)	Concentration [mean, (range), max.]	Reference"
USA	Usually < 10	2
USA	17.9 (0.01-800)	3
LAKE WATER (μg/L)		
Dissolved solids		
< 2,000 mg/L	(0.0–100)	6
> 2,000 mg/L	(0.0–2,000)	6
Lake Superior	(0.1–1.6)	6
Japan, various	(0.2–1.9)	6
Germany, Elbe River	(20-25)	6
Searles Lake, California	(198,000–243,000)	1, 4
California, other lakes	(0.0–100)	1, 4
Michigan	Max. 2.4	1, 4
Wisconsin	(44117)	1, 4
Florida	3.6	1, 4
Lake Chautauqua, New York	(3.5–35.6)	1, 4
Lake Ohakuri, New Zealand	(30–60)	7
Finfeather Lake, Texas	Max. 240,000	8
Thermal waters, worldwide	(20-3800 usually), Max. 276,000	1–3, 9
RAIN (μg/L)		
Canada	(0.01-5)	3
Rhode Island	0.8	1
Seattle, Washington	17.0	1
RIVER WATER (μg/L)		
Polluted, IJSA	Max. 6,000	4
Nonpolluted, USA	Usually < 5	4
Nationwide, USA, 1974-1981		
25th percentile	< 1	10
50th percentile	1	10
75th percentile	3	10
ROCK (mg/kg)		
Limestone	1.7 (0.1-20)	1
Sandstone	2 (0.6–120)	1
Shale and clay	14.5 (0.3-490)	1
Phosphate	22.6 (0.4–188)	1
Igneous, various	1.5-3 (0.06–113)	1
SEAWATER (μg/L)		
Worldwide	2 (0.15-6)	6
Pacific Ocean	(1.441.8)	11
Atlantic Ocean	(1.0–1.5)	11
South Australia		
Total dissolved As	1.3 (1.1–1.6)	12
As^{+5}	1.29	12

Table *1 (Continued)*

Material (concentration unit)	Concentration [mean, (range), max.]	Reference"
As^{+3}	0.03	12
Particulate As	< 0.0006	12
UK, Beaulieu Estuary		
Water temperature < 12 °C		
Inorganic arsenic	(0.4-0.9)	13
Suspended arsenic	(0.02-0.24)	13
Organoarsenicals	(0.19-0.75)	13
Water temperature > 12 °C		
Inorganic arsenic	(0.6–1.1)	13
Suspended arsenic	(0.2-0.6)	13
Organoarsenicals	ND	13
SEDIMENTS (mg/kg dry weight)		
Near sewer outfall	35	3
From areas contaminated by smelters, arsenical herbicides, or mine tailings		
Surface	(198-3500)	1, 7, 9, 14, 15
Subsurface	(12-25)	1, 7, 9, 14, 15
Upper Mississippi River	2.6 (0.6–6.2)	16
Lake Michigan	(5–30)	1
Naturally elevated	> 500	1, 9
Oceanic	33.7 (< 0.4-455)	3
Lacustrine	(Usually 5–26.9), max. 13,000	3
SNOW (mg/kg)		
Near smelter	> 1000	3
SOIL POREWATERS (μg/L)		
Mineralized areas		
Arsenate	(79-210)	17
Arsenite	(2–11)	17
Monomethyl arsonic acid (MMAA)	(4422)	17
Total arsenic	(93-240)	17
Unmineralized areas		
Arsenate	(18-49)	17
Arsenite	(1-7)	17
MMAA	< 1	17
Total arsenic	(13–59)	17
SOILS (mg/kg dry weight)		
USA, uncontaminated	7.4	18
Worldwide, uncontaminated	7.2	18
Canada		
Near gold mine		
Air levels 3.9 μg As/m^3	21,213	3
80 km distant	(10-25)	3

Table 1 *(Continued)*

Material (concentration unit)	Concentration [mean, (range), max.]	Reference"
Near smelter		
Japan	Max. 2470	2
Tacoma, Washington	Max. 380	2
Treated with arsenical pesticides		2
USA	165 (l-2553)	6
Canada	121	6
SYNTHETIC DETERGENTS (mg/kg)		
Household, heavy duty	(1–73)	1, 2

"1, NAS (1977); 2, Pershagen and Vahter (1979); 3, NRCC (1978); 4, EPA (1980); 5, Hood (1985); 6, Woolson (1975); 7, Freeman et al. (1986); 8, Sorensen et al. (1985); 9, Farmer and Lovell (1986); 10, Smith et al. (1987); 11, Sanders (1980); 12, Maher (1985a); 13, Howard et al. (1984); 14, Hallacher et al. (1985); 15, Takamatsuet al. (1985); 16, Wieneret al. (1984); 17, Haswell et al. (1985); 18, Dudas (1984).

acid and dimethylarsinic acid, and these are usually present in lower concentrations than inorganic arsenites and arsenates (Pershagen and Vahter, 1979). Total arsenic concentrations in surface water and groundwater are usually < 10 $\mu g/L$; in certain areas, however, levels above 1 mg/L have been recorded (Pershagen and Vahter, 1979).

In air, most arsenic particulates consist of inorganic arsenic compounds, often as As^{+3}. Burning of coal and arsenic-treated wood and smelting of metals are major sources of atmospheric arsenic contamination (i.e., > 1 $\mu g/m^3$); in general, atmospheric arsenic levels are higher in winter, due to increased use of coal for heating (Pershagen and Vahter, 1979).

The main carrier of arsenic in rocks and in most types of mineral deposits is iron pyrite (FeS_2), which may contain > 2000 mg/kg of arsenic (NRCC, 1978). In localized areas, soils are contaminated by arsenic oxide fallout from smelting of ores (especially sulfide ores) and combustion ofarsenic-rich coal (Woolson, 1975).

Arsenic in lacustrine sediment columns is subject to control by diagenetic processes and adsorption mechanisms, as well as anthropogenic influences (Farmer and Lovell, 1986). For example, elevated levels of arsenic in or near surface sediments may have several causes (Farmer and Lovell, 1986), including natural processes (Loch Lomond, Scotland) and human activities such as smelting (Lake Washington, Washington; Kelly Lake, Ontario, Canada), manufacture of arsenical herbicides (Brown's Lake, Wisconsin), and mining operations (Northwest Territories, Canada). Elevated levels of arsenic in sediments of the Wailoa River, Hawaii, are the result of As_2O_3 applied as an antitermite agent between 1932 and 1963 (Hallacher et al., 1985). These elevated levels are found mainly in anaerobic sediment regions where the chemical has been relatively undisturbed by activity. Low levels of arsenic in the biota of the Wailoa River estuary suggest that arsenic is trapped in the anaerobic sediment layers.

Arsenic geochemistry in Chesapeake Bay, Maryland, depend on anthropogenic inputs and phytoplankton species composition (Sanders, 1985). Inputs of anthropogenic arsenic into Chesapeake Bay are estimated at 100 kg daily or 39 tons/year-probably from sources such as unreported industrial discharges, arsenical herbicides, and wood preservatives (Sanders, 1985). The chemical form of the arsenic in solution varies seasonally and along the axis of the bay. Arsenic is present only as arsenate in winter, but substantial quantities of reduced and methylated forms are present in summer in different areas. The forms and distribution patterns of arsenic during summer suggest that separate formation processes exist. Arsenite, present in low-salinity regions, may have been formed by chemical, reduction in anoxic, subsurface waters and then mixed into the surface layer, Methylated arsenicals are highly correlated with standing crops of algae. One particular form, methylarsonate, is significantly correlated with the dominant alga Chroomonas. Since arsenic reactivity and toxicity are altered by transformation of chemical form, observed variations in arsenic speciation have considerable geochemical and ecological significance (Sanders, 1985).

5.2. Biological Samples

Background arsenic concentrations in living organisms are usually < 1 mg/kg fresh weight in terrestrial flora and fauna, birds, and freshwater biota. These levels are higher, sometimes markedly so, in biota collected from mine waste sites and arsenic-treated areas, and near smelters and mining areas, areas with high geothermal activity, and manufacturers of arsenical defoliants and pesticides (Table 2). For example, bloaters (*Coregonus hoyi*) collected in Lake Michigan near a facility that produced arsenical herbicides consistently had the highest (1.5–2.9 mg As/kg fresh weight whole body) arsenic concentrations measured in freshwater fishes in the United States between 1976 and 1984 (Schmitt and Brumbaugh, 1990). Marine organisms, however, normally contain arsenic residues of several to more than 100 mg/kg dry weight (Lunde, 1977); however, as will be discussed later, these concentrations present little hazard to the organism or its consumers.

Shorebirds (seven species) wintering in the Corpus Christi, Texas, area contained an average of only 0.3 mg As/kg fresh weight in their livers (maximum of 1.5 mg/kg), despite the presence of smelters and the heavy use of arsenical herbicides and defoliants; these values probably reflect normal background concentrations (White et al., 1980). Similar arsenic levels were reported in the livers of brown pelicans (*Pelecanus occidentalis*) collected from South Carolina (Blus et al., 1977). The highest arsenic concentration recorded in seemingly unstressed coastal birds was 13.2 mg/kg fresh weight lipids (Table 2). This observation tends to corroborate the findings of others that arsenic concentrates in lipid fractions of marine plants, invertebrates, and higher organisms. An abnormal concentration of 16.7 mg As/kg fresh weight was recorded in the liver of an osprey (*Pandion haliaetus*) from the Chesapeake Bay region (Wiemeyer et al., 1980). This bird was alive but weak, with serious histopathology including

Table 2 Arsenic Concentrations in Field Collections of Selected Species of Flora and Fauna

Ecosystem, Species, and Other Variables	Concentration (mg As/kg FW or DW[a]), in ppm [mean, (range), max.]	Reference[b]
TERRESTRIAL PLANTS		
Colonial bentgrass, ***Agrostis tenuis***		
On mine waste site	1480 DW, max. 3470 DW	1
On low-arsenic soil	(0.3-3) DW	1
Scotch heather, *Calluna vulgaris*		
On mine waste site	1260 DW	1
On low-arsenic soil	0.3 DW	1
Coontail, ***Ceratophyllum demersum***		
From geothermal area, New Zealand	(20–1060) DW	1
Cereal grains		
From arsenic-treated areas	Usually < 3 DW, max. 252 DW	2
Nontreated areas	Usually < 0.5 DW, max. 5 DW	2
Grasses		
From arsenic-treated areas	(0.5–60,000) DW	2
Nontreated areas	(0.1–0.9) DW	2
Apple, ***Malus sylvestris***		
Fruit	< 0.1 FW, < 1.8 DW	1
Alfalfa, *Medicago sativa*		
USA	1.6 FW	1
Montana, smelter area	(0.4-5.7) FW	1
White spruce, ***Picea alba***		
Arsenic-contaminated soil		
Branch	(2.8–14.3) DW	1
Leaf	(2.1–9.5) DW	1
Trunk	(0.3-55) DW	1
Root	(45–130) DW	1
Control site		
All samples	< 2.4 DW	1
Pine, ***Pinus*** silvestrus, needles		
Near USSR metals smelter; soil levels 120 mg As/kg	22 FW	3
Trees		
Nontreated areas	Usually < 1 DW	2
Lowbush blueberry, *Vaccinum angustifolium*		
Maine, leaf		
Arsenic-treated soil	(6.8–15) DW	1
Control	0.8 DW	1
Various species		1
From uncontaminated soils	(< 0.01-5) DW	2
From arsenic-impacted (80 mg/kg) soils	1.2 (< 0.2–5.8) DW	4

[a,b] See page 213 for footnotes.

Table 2 *(Continued)*

Ecosystem, Species, and Other Variables	Concentration (mg As/kg FW or DW[a]), in ppm [mean, (range), max.]	Reference[b]
Vegetables		
From arsenic-treated areas	Usually < 3 DW, max. 145 DW	2
Nontreated areas	Usually < 1 DW, max. 8 DW	2
Vegetation		
Near gold mine, Canada, air levels up to 3.9 $\mu g\ As/m^3$	Max. 11,438 DW	5
80 km distant	(12-20) DW	5
FRESHWATER FLORA		
Aquatic plants		
Arsenic-treated areas	**(20-1450)** DW	2
Untreated areas	(1.4413) DW	2
Irish moss, ***Chondrus crispus***		2
Whole	(5–12) DW	1
Pondweeds, ***Potamogeton*** spp.		1
Whole		
Near geothermal area	(11-436) DW	1
Control site	< 6 DW	1
Widgeongrass, ***Ruppia maritima,*** from Kern National Wildlife Refuge, California, contaminated by agricultural drainwater of 12–190 $\mu g\ As/L$	Max. 430 DW	6
FRESHWATER FAUNA		
Alewife, ***Alosa pseudoharengus***		
Whole, Michigan	**0.02** FW	1
Muscle, Wisconsin	0.0 FW	1
White sucker, ***Catostomus commersoni***		1
Muscle	(0.03–0.13) FW	1
Whole	(0.05–0.16) FW	1
Common carp, *Cyprinus* ***carpio***		
Upper Mississippi River, 1979		
Whole	0.4 (0.2–0.6) DW	7
Liver	**0.4** (0.3–1) DW	7
Nationwide, USA		
Whole	0.05 FW	1
Muscle	**(0.0C0.2)** FW	1
Northern pike, *Esox lucius*		
Muscle		
Canada	**(0.05-0.09)** FW	1
Great Lakes	< **0.05** FW	1
Sweden	**0.03** FW	1
New York	< 0.1 FW	1
Wisconsin	< 0.01 FW	1

Table 2 *(Continued)*

Ecosystem, Species, and Other Variables	Concentration (mg As/kg FW or DW"), in ppm [mean, (range), max.]	Reference[b]
Fish, various species		
Whole	Max. 1.9 FW	2
Whole	(0.04–0.2) FW	8
Netherlands, 1977– 1984, muscle	(0.04-0.2) FW	9
Nationwide, USA, whole fish		
1976–1977	0.27 FW, max. 2.9 FW	10, 11
1978-1979	0.16 FW, max. 2.1 FW	11
1980–1981	0.15 FW, max. 1.7 FW	11
1984	0.14 FW, max. 1.5 FW	11
Near smelter (water arsenic 2.3-2.9 μg/L)		
Muscle, 3 species		
Total arsenic	(0.05-0.24) FW	12
Inorganic arsenic	(0.01-0.02) FW	12
Liver, 2 species		
Total arsenic	0.15 FW	12
Inorganic arsenic	0.01 FW	12
Control location (water arsenic < 0.5 μg/L)		
Muscle		
Total arsenic	(0.06-0.09) FW	12
Inorganic arsenic	< 0.03 FW	12
Liver		
Total arsenic	0.09 FW	12
Inorganic arsenic	< 0.01 FW	12
Channel catfish, *Ictalurus punctatus*		
Muscle		
Native	(0.0-0.3) FW	1
Cultured	(0.2-3.1) FW	1
Whole, nationwide	(< 0.05-0.3) FW	1
Green sunfish, *Lepomis cynellus*, liver		
Polluted waters (from manufacturer of arsenical defoliants and pesticides), Texas. **Mean** water concentration 13.5 mg As/L; sediment content of 4700 mg/kg		
Age 1 to 2	(19.7-64.2) DW	13
Age 3	15 DW	13
Age ≥ 4	(6.1-11.5) DW	13
Bluegill, *Lepomis macrochirus*		
From pools treated with arsenic		
Muscle	1.3 FW	1
Skin and scales	2.4 FW	1

Table 2 *(Continued)*

Ecosystem, Species, and Other Variables	Concentration (mg As/kg FW or DW[a]), in ppm [mean, (range), max.]	Reference[b]
Gills and GI tract	17.6 FW	1
Liver	11.6 FW	1
Kidney	***5.9*** FW	1
Ovary	***8.4*** FW	1
Control locations		
All tissues	***< 0.2*** FW	1
Whole		
Nationwide, USA	(< 0.05–0.15) FW	1
Upper Mississippi River, 1979	0.3 (0.2–0.4) DW	7
Smallmouth bass, ***Micropterus dolomieui***		
Muscle		
Wisconsin	< 0.13 FW	1
Lake Erie	***0.22*** FW	1
New York	(0.03-0.51) FW	1
Whole, nationwide, USA	***(< 0.05-0.28)*** FW	1
Largemouth bass, ***Micropterus salmoides***		
Whole, nationwide, USA	(< 0.05–0.22) FW	1
Muscle		
Wisconsin	(0.0-0.12) FW	1
New York	(0.03-0.16) FW	1
Striped bass, ***Morone saxatilis***		
Muscle	(0.2-0.7) FW	1
Coho salmon, ***Oncorhynchus kisutch***		
Muscle		
Wisconsin	< 0.15 FW	1
Lake Erie	(< 0.07-0.17) FW	1
New York	***< 0.5*** FW	1
USA	0.09 FW	1
Rainbow trout, ***Oncorhynchus mykiss***		
All tissues	***< 0.4*** FW	1
Yellow perch, *Perca flavescens*		
All tissues	< 0.16 FW	1
Atlantic salmon, *Salmo salar*		
Oil		
Liver	6.7 FW	1
Muscle	(0.8 -3.1) FW	1
Lake trout, ***Salvelinus namaycush***		
Whole, nationwide, USA	(0.06–0.68) FW	1
MARINE FLORA		
Algae		
Green	***(0.05-5)*** DW	2

Table 2 (Continued)

Ecosystem, Species, and Other Variables	Concentration (mg As/kg FW or DW"), in ppm [mean, (range), max.]	Reference[b]
Brown	Max. 30 DW	2
11 species	(2-58) DW	14
Various species	(10-100) DW	15
Seaweed, ***Chondrus*** *crispus*	5.2 DW	2
Alga, Fucus spp.		
Oil	(6–27) FW	2
Fatty acid	(5-6) FW	2
Brown alga, ***Fucus*** *vesiculosus*		
Whole	(35–80) DW	1
Brown alga, ***Laminaria digitata***		
Whole	94 DW	2
Whole	(42-50) DW	1
Oil	(155-221) DW	2
Fatty acid	(8-36) DW	2
Alga, ***Laminaria hyperborea***		
Tot al arsenic	142 DW	14
Organic arsenic	139 DW	14
Periphyton, Louisana, USA	8.4 DW	16
Sargassum weed, *Sargassum fluitans*		
Total arsenic	19.5 FW	8
As^{+3}	1.8 FW	8
As^{+5}	17.7 FW	8
Organoarsenicals	0.2 FW	8
Seaweed, ***Sargassum*** sp.		
Total arsenic	(4.1-8.7) FW	5
As^{-3}	(0.14-0.35) FW	5
As^{-5}	(1.9-7.3) FW	5
Organoarsenicals	Max. 0.1 FW	5
Seaweeds		
Whole	(4-94) DW	2
Whole	(10-109) DW	14
Oil fraction	(6-221) FW	14
MARINE MOLLUSKS		
Bivalves, California, 1984– 1986, soft parts		
Clam, ***Corbicula*** sp.	5.4– 11.5 DW	17
Clam, *Macoma balthica*	7.6-12.1 DW	17
Ivory shell, ***Buccinum striatissimum***		
Muscle		
Total arsenic	38 FW	18
Arsenobetaine	24.2 FW	18
Midgut gland		18
Total arsenic	18 FW	18
Arsenobetaine	10.8 FW	18

Table 2 *(Continued)*

Ecosystem, Species, and Other Variables	Concentration (mg As/kg FW or DW"), in ppm [mean, (range), max.]	Reference'
Oysters, ***Crassostrea*** spp.		
Soft parts	(1.3–10) DW, (0.3-3.4) FW	14
American oyster, ***Crassostrea uirginica***		
Soft parts	2.9 FW	1
Soft parts	10.3 DW	19
Spindle shells, *Hemifusus* spp.		
Hong Kong 1984, muscle		
Total arsenic	Max. 500 FW	20
Inorganic arsenic	< 0.5 FW	20
Limpet, ***Littorina littorea***		
Soft parts		
Near arsenic source	11.5 DW	14
Offshore	4 D W	14
Squid, *Loligo* ***vulgar-is***		
Soft parts	(0.8-7.5) FW	1
Hardshell clam, ***Mercenaria mercenaria***		
Soft parts		
Age 3 years	3.8 DW	14
Age 4 years	4.7 DW	14
Age 10 years	9.3 DW	14
Age 15 years	8.4 DW	14
Mollusks, edible tissues		
Hong Kong, 1976– 1978		
Bivalves	(3.2-39.6) FW	21
Gastropods	(199176) FW	21
Cephalopods	(0.7–5.5) FW	21
USA		
6 species	(2-3) FW	22
8 species	(3–4) FW	22
3 species	(4-5) FW	22
4 species	(7-20) FW	22
Yugoslovia, northern Adriatic Sea, summer 1986		
6 species	21-31 FW	23
Mussel, ***Mytilus edulis***		
Soft parts	2.5 (1.4-4.6) FW	9
Soft parts	(1.6-16) DW	14
Mussels, Louisiana, USA		
Soft parts	1.444.5 DW	16
Scallop, ***Placopecten magellanicus***		
Soft parts	1.6 (1.332.4) FW	1

Table 2 *(Continued)*

Ecosystem, Species, and Other Variables	Concentration (mg As/kg FW or DW"), in ppm [mean, (range), max.]	Reference[b]
MARINE CRUSTACEANS		
Blue crab, *Callinectes sapidus*		
Florida, whole	7.7 FW	1
Maryland, soft parts	(0.55 1.8) FW	1
Dungeness crab, ***Cancer magister***		
Muscle	6.5 (2.2-37.8) FW	1
Muscle	4 F W	24
Alaskan snow crab, ***Chionocetes hairdii***		
Muscle	7.4 FW	24
Copepods, whole	(2–8.2) DW, (0.4-I .3) FW	14
Shrimp, ***Crangon crangon***		
Netherlands, 1977– 1984		
Muscle	3 (226.8) FW	9
Crabs and shrimps,		
Louisiana, USA		
Muscle	< 0.2 DW	16
Crustaceans, edible tissues		
Hong Kong, 197661978		
Crabs	(5.4-19.1) FW	21
Lobsters	(26.7–52.8) FW	21
Prawns and shrimps	(1.2-44) FW	21
USA		
6 species	(3-5) FW	22
3 species	(5– 10) FW	22
4 species	(10-20) FW	22
2 species	(20-30) FW	22
1 species	(40–50) FW	22
American lobster, ***Homarus americanus***		
Muscle	(3.8-7.6) DW, max. 40.5 FW	1
Hepatopancreas	22.5 FW	1
Whole	(3.8% 16) DW, (1-3) FW	14
Lesser spider crab, *Maia* ***crispata***		
Yugoslavia, 1986		
Digestive gland	25.4437.1 FW	23
Muscle	24.5-28.0 FW	23
Stone crab, ***Menippe*** *mercenaria*		
Whole	(9– 11.8) FW	1
Deep-sea prawn, *Pandalus* ***borealis***		
Head and shell	68.3 DW	1

Table *2 (Continued)*

Ecosystem, Species, and Other Variables	Concentration (mg As/kg FW or DW"), in ppm [mean, (range), max.]	Reference[b]
Muscle	61.6 DW	1
Oil	42 DW, 10.1 FW	1
Egg	3.7-14 FW	1
Prawns, *Pandalus* spp.		
Whole	(7.3-11.5) FW	14
Alaskan king crab, ***Paralithodes camtschatica***		
Muscle	8.6 FW	24
Brown shrimp, ***Penaeus*** *aztecus*		
Muscle	(3.1-5.2) FW	1
Whole	0.6 DW	1
White shrimp, ***Penaeus*** *setiferus*		
Muscle		
Mississippi	(1.7-4.4) FW	1
Florida	(2.8-7.7) FW	1
Shrimp, ***Sergestes*** *lucens*		
Muscle		
Total arsenic	5.5 FW	25
Arsenobetaine	4.5 FW	25
Shrimps		
Exoskeleton	15.3 FW	8
Muscle, 2 species	(18.8-41.6) FW, max. 128 DW	2
MARINE FISHES AND ELASMOBRANCHS		
Whitetip shark, ***Carcharhinus*** *longimanus*		
Muscle	3.1 FW	26
Black sea bass, ***Centropristis striata***		
Muscle	6.4 DW	1
Peacock wrasse, *Crenilabrus pavo*, Yugoslovia, 1986		
Liver	26.9-37.6 FW	23
Muscle	20.7-22.2 FW	23
Elasmobranchs		
Muscle		
Sharks	Max. 30 FW	14
Rays	Max. 16.2 FW	14
Roundnose flounder, ***Eopsetta grigorjewi***		
Muscle	20.1 FW	27
Finfishes		
Near metal smelter,		

Table 2 (Continued)

Ecosystem, Species, and Other Variables	Concentration (mg As/kg FW or DW[a]), in ppm [mean, (range), max.]	Reference[b]
water concentration		
2.3-2.9 μg As/L		
Muscle, 6 species		
Total arsenic	(0.2-2.6) FW	12
Inorganic arsenic	(0.02–0.1) FW	12
Liver, 4 species		
Total arsenic	(0.4–1.8) FW	12
Inorganic arsenic	(0.02-0.07) FW	12
Control location, water concentration < 2.0 μg As/L		
Muscle, 5 species		
Total arsenic	(0.1-1.2) FW	12
Inorganic Arsenic	(0.02–0.15) FW	12
Liver, 4 species		
Total arsenic	(0.2–1.5) FW	12
Inorganic arsenic	(0.02–0.05) FW	12
Finfish, Hong Kong, 1976–1978		
Edible tissues	Max. 21.1 FW	21
Finfish, Netherlands, 1977–1984		
Muscle, 4 species	(2.8–10.9) FW	9
Finfish, North America		
Liver		
49 species	(0.7-5) FW	22
26 species	(5-20) FW	22
6 species	(20–50) FW	22
Muscle		
91 species	(0.6-4) FW	22
41 species	(4-8) FW	22
27 species	(8-30) FW	22
6 species	0.2 (0.18–0.30) DW	16
4 species		
Total arsenic	(1.4-10) FW	28
Inorganic arsenic	< 0.5 FW	28
Whole		
16 species	(1-8) FW	22
Finfish, worldwide		
Various tissues		
Total arsenic	Max. 142FW	2
Inorganic arsenic	(0.7–3.2) FW	2
Organic arsenic	(3.4–139) FW	2
Atlantic cod, *Gadus morhua*		
Muscle	2.2 FW	2
Liver	9.8 FW	2

Table 2 *(Continued)*

Ecosystem, Species, and Other Variables	Concentration (mg As/kg FW or DW[a]), in ppm [mean, (range), max.]	Reference[b]
Blue pointer, *Isurus oxyrhinchus*		
Muscle	9.5 FW	**26**
Striped bass, ***Morone sasatilis***		
Muscle	***(0.3-0.5)*** FW, 1.8 DW	14
Liver	0.7 FW	14
Striped mullet, *Mugil cephalus*		
Viscera	Max. 1.3 FW	29
English sole, *Parophrys vetulus*		
Muscle	1.1. (0.6-l 1.5) FW	
Skate, *Raja* sp.		
Muscle	16.2 FW	
Windowpane flounder, *Scopthalmus aquosus*		
Muscle	(1.4-2.8) FW	
Spiny dogfish, ***Syualus acanthias***		
Muscle	10 DW	**30**
Liver	5.7 DW	**30**
Spleen	**9.8** DW	**30**
Yolk sac	9.1 DW	**30**
Embryo	**2.4** DW	**30**
AMPHIBIANS AND REPTILES		
Alligator, *Alligator* ***mississipiensis***		
Egg	***(0.05-0.2)*** FW	
Crocodile, *Crocodylus acutus*		
Egg	**0.2** FW	31
Frogs, *Rana* spp.		
All tissues	< 0.4 FW	
Toads, 2 species		
All tissues	< 0.05 FW	
BIRDS		
American black duck, ***Anus rubripes***		
Egg	**0.2** FW	14
Ducks, *Anas* spp.		
All tissues	< 0.4 FW	
Scaup, ***Aythya*** spp.		
All tissues	< 0.4 FW	
Gulls, 3 species		
Oil	(0.6 – 13.2) FW	14
Osprey, *Pandion* ***haliaetus***		
Liver	Max. 16.7 FW	32
Brown pelican, *Pelecanus* ***occidentalis***		
Egg		
South Carolina, 1971 – 1972	***0.3 (0.08-0.8)*** FW	**33**

Table *2 (Continued)*

Ecosystem, Species, and Other Variables	Concentration (mg As/kg FW or DW"), in ppm [mean, (range), max.]	Reference[b]
Florida, 1969-1970	0.1 (0.07-0.2) FW	33
Liver, 1972– 1973, GA, FL, SC		
Found dead	(0.2– 1) FW	33
Shot	(0.3–0.9) FW	33
Shorebirds		
Corpus Christi, Texas, 1976– 1977		
Liver, 7 species	(0.05– 1.5) FW	34
New Zealand, 5 species		
Feather	< l F W	14
Liver	Max. 2.6 FW	14
Starling, *Sturnus vulgaris*		
Whole, nationwide, USA, 1971	(< 0.01–0.21) F W	2
Icelandic redshank, *Tringa totanus robusta*		
Netherlands, 1979– 1982		
Feather		
Juveniles	Max. 0.8 FW	35
Adults	(0.5–3.2) FW	35
MAMMALS		
Fin whale, *Balaenoptera physalis*		
Blubber oil	1.8 FW	1
Cow, *Bos* bovis		
Downwind from copper smelter		
16-21 km		
Hair	8.9 FW	
Milk	0.013 FW	
Blood	0.026 FW	
60 km		
Hair	0.46 FW	
Milk	0.002 FW	
Blood	0.009 FW	
Controls		
Milk	< 0.001 F W	36
Muscle	0.005 FW	36
Liver	(0.008-0.012) FW	36
Kidney	(0.017-0.053) FW	36
Domestic animals		
All tissues	< 0.3 FW	2
Livestock		
All tissues	< 0.6 FW	2
Marine mammals		14
Pinnipeds		
All tissues	Max. 1.7 FW	14

Table 2 (Continued j

Ecosystem, Species, and Other Variables	Concentration (mg As/kg FW or DW"), in ppm [mean, (range), max.]	Reference'
Cetaceans		
Muscle	0.4 DW	14
Oil	(0.6-2.8) FW	14
White-tailed deer, *Odocoileus virginianus* Tennessee, killed from arsenic herbicide		
Liver	19FW	1
Kidney	17.8 FW	1
Rumen contents	22.5 FW	1
Harbor seal, *Phoca vitulina*		
UK, all tissues	< 0.3 FW	1
Fox, *Vulpes* sp.		
All tissues	< 0.7 FW	1
Wildlife		
All tissues	< 1 FW	2

[a] Abbreviations: DW = dry weight; FW = fresh weight.

[b] 1, Jenkins (1980); 2, NAS (1977); 3, Mankovska (1986); 4, Merry et al. (1986); 5, NRCC (1978); 6, Camardese et al. (1990); 7, Wiener et al. (1984); 8, Woolson (1975); 9, Vos and Hovens (1986); 10, Lima et al. (1984); 11, Schmitt and Brumbaugh (1990); 12, Norin et al. (1985); 13, Sorensen et al. (1985); 14, Eisler (1981); 15, Pershagen and Vahter (1979); 16, Ramelow et al. (1989); 17, Johns and Luoma (1990); 18, Shiomi et al. (1984a); 19, Zaroogian and Hoffman (1982); 20, Phillips and Depledge (1986); 21, Phillips et al. (1982); 22, Hall et al. (1978); 23, Ozretic et al. (1990); 24, Francesconi et al. (1985); 25, Shiomi et al. (1984b); 26, Hanaoka and Tagawa, (1985a); 27, Hanaoka and Tagawa, (1985b); 28, Reinkeet al. (1975); 29, Hallacher et al. (1985); 30, Windom et al. (1973); 31, Hall (1980); 32, Wiemeyer et al. (1980); 33, Blus et al. (1977); 34, White et al. (1980); 35, Goede, (1985); 36, Vreman et al. (1986).

absence of subcutaneous fat, presence of serous fluid in the pericardial sac, and disorders of the lung and kidney. The bird died shortly after collection. Arsenic concentrations in the livers of other ospreys collected in the same area usually were < 1.5 mg As/kg fresh weight.

Arsenic concentrations in the tissues of marine biota show a wide range of values, being highest in lipids, liver, and muscle tissues, and varying with age of the organism, geographic locale, and proximity to anthropogenic activities (Table 2). In general, tissues with high lipid content contain high levels of arsenic. Crustacean tissues sold for human consumption and collected in U.S. coastal waters usually contain 3 to 10 mg As/kg fresh weight (Hall et al., 1978) or 1 to 100 mg/kg dry weight (Fowler and Unlu, 1978), and are somewhat higher than those reported for finfish and molluskan tissues. Marine finfish tissues usually contain 2 to 5 mg As/kg fresh weight (Table 2). However, postmortem reduction of As^{+5} to As^{+3} occurs rapidly in fish tissues (Reinke et al., 1975), suggesting a

need for additional research in this area. Maximum arsenic values recorded in elasmobranchs (mg/kg fresh weight) were 30 in the muscle of a shark, *Mustelus* antarcticus, and 16.2 in the muscle of a ray, *Raja* sp. (Eisler, 1981). The highest arsenic concentration recorded in a marine mammal, 2.8 mg As/kg fresh weight lipid, was from a whale (Eisler, 198 1).

Arsenic appears to be elevated in marine biota because of their ability to accumulate arsenic from seawater and food sources, not because of localized pollution (Maher, 1985b). The great majority of arsenic in marine organisms exists as water-soluble and lipid-soluble organoarsenicals, including arsenolipids, arsenosugars, arsenocholine, arsenobetaine $[(CH_3)_3AsCH_2COOH]$, monomethylarsonate $[CH_3AsO(OH)_2]$, and dimethylarsinate $[(CH_3)_2AsO(OH)]$, as well as other forms. There is no convincing hypothesis to account for the existence of all the various forms of organoarsenicals found in marine organisms. One hypothesis is that each form involves a single metabolic pathway concerned with the synthesis and turnover of phosphatidylcholine (Phillips and Depledge, 1986). Arsenosugars (arsenobetaine precursors) are the dominant arsenic species in brown kelp, *Ecklonia radiata;* giant clam, *Tridacna maxima;* shrimp, *Pandalus borealis;* and ivory shell, *Buccinum striatissimum* (Shiomi et al., 1984a, b; Francesconi et al., 1985; Matsuto et al., 1986; Phillips and Depledge, 1986). For most marine species, however, there is general agreement that arsenic exists primarily as arsenobetaine, a water-soluble organoarsenical that has been identified in the tissues of western rock lobster (*Panulirus* Cygnus), American lobster (*Homarus americanus),* octopus *(Paroctopus* sp.), sea cucumber (Stichopus *japonicus*), blue shark *(Prionace gluaca*), sole (*Limanda* sp.), squid *(Sepioteuthis australis*), prawn (Penaeus *latisulcatus*), scallop (*Pecten alba*), and many other species, including teleosts, mollusks, tunicates, and crustaceans (Shiomi et al., 1984b; Francesconi et al., 1985; Hanaoka and Tagawa, 1985a, b; Maher, 1985b; Norin et al., 1985; Matsuto et al., 1986; Ozretic et al., 1990; Phillips, 1990). The potential risks associated with consumption of seafoods containing arsenobetaine seem to be minor. The chemical was not mutagenic in the bacterial *Salmonella typhimurium* assay (Ames test), had no effect on metabolic inhibition of Chinese hamster ovary cells at 10,000 mg/L, and showed no synergism or antagonism on the action of other contaminants (Jongen et al., 1985). Arsenobetaine was not toxic to mice at oral doses of 10,000 mg/kg body weight during a 'I-day observation period, and it was rapidly absorbed from the gastrointestinal tract and rapidly excreted in urine without metabolism, owing to its high polar and hydrophylic characteristics (Kaise et al., 1985).

6. LETHAL AND SUBLETHAL EFFECTS

As will be discussed later, most authorities agree on 10 points: (1) inorganic arsenicals are more toxic than organic arsenicals, and trivalent forms are more toxic than pentavalent forms; (2) episodes of arsenic poisoning are either acute or subacute; cases of chronic arsenosis are rarely encountered, except in humans; (3)

sensitivity to arsenic is greatest during the early developmental stages; (4) arsenic can traverse placental barriers; as little as 1.7 mg As^{+5}/kg body weight at critical stages of hamster embryogenesis, for example, can produce fetal death and malformation; (5) biomethylation is the preferred detoxification mechanism for inorganic arsenicals; (6) arsenic is bioconcentrated by organisms, but not biomagnified in the food chain; (7) in soils, depressed crop yields were recorded at 3 to 28 mg water-soluble As/L, or about 25 to 85 mg total As/kg soil; adverse effects on vegetation were recorded at concentrations in air $> 3.9\ \mu g\ As/m^3$; (8) some aquatic species were adversely affected at water concentrations of 19 to 48 μg As/L, or 120 mg As/kg in the diet, or tissue residues of 1.3 to 5 mg As/kg fresh weight; (9) sensitive species of birds died following single oral doses of 17.4 to 47.6 mg As/kg body weight; and (10) adverse effects were noted in mammals at single oral doses of 2.5 to 33 mg As/kg body weight, at chronic oral doses of 1 to 10 mg As/kg body weight, and at feeding levels of 50 mg-and sometimes only 5 mg- As/kg in the diet.

The literature emphasizes that arsenic metabolism and toxicity vary greatly among species and that its effects are significantly altered by numerous physical, chemical, and biological modifiers. Adverse health effects, for example, may involve the respiratory, gastrointestinal, cardiovascular, and hematopoietic systems, and may range from reversible effects to cancer and death, depending in part on the physical and chemical forms of arsenic tested, the route of administration, and the dose.

6.1. Carcinogenesis, Mutagenesis, and Teratogenesis

Epidemiological studies show that an increased risk of cancers in the skin, lung, liver, lymph, and hematopoietic systems of humans is associated with exposure to inorganic arsenicals. These increased cancer risks are especially prevalent among smelter workers and those engaged in the production and use of arsenical pesticides where atmospheric levels exceed 54.6 $\mu g\ As/m^3$ (NRCC, 1978; Belton et al., 1985; Pershagen and Bjorklund, 1985). Skin tumors, mainly of low malignancy, have been reported after consumption of arsenic-rich drinking waters; a total dose of several grams, probably as As^{+3}, is usually required for the development of skin tumors (Pershagen and Vahter, 1979). High incidences of skin cancer and hyperpigmentation were noted among several population groups, especially Taiwanese and Chileans, who consumed water containing more than 0.6 mg As/L; the frequency of cancer was highest among people over age 60 who demonstrated symptoms of chronic arsenic poisoning (NRCC, 1978).

Arsenic reportedly inhibits cancer formation in species having a high incidence of spontaneous cancers (NRCC, 1978). In fact, arsenic may be the only chemical for which there is sufficient evidence of carcinogenicity in humans but not in animals (Woolson, 1975; Belton et al., 1985; Lee et al., 1985). In general, animal carcinogenicity tests with inorganic and organic arsenicals have been negative (Hood, 1985), even when the chemicals were administered at or near the highest tolerated dosages for long periods (NAS, 1977). Most studies of arsenic carcino-

genesis in animals were presumably of insufficient duration to simulate conditions in long-lived species such as humans (NRCC, 1978). However, mice developed leukemia and lymphoma after 20 subcutaneous injections of 0.5 mg As^{+5}/kg body weight; 46% of the experimental group developed these signs, versus none of the controls (NRCC, 1978). Pulmonary tumorogeniciry has been demonstrated in hamsters administered calcium arsenate intratracheally (Pershagen and Bjorklund, 1985). Cacodylic acid and other organoarsenicals are not carcinogenic, but may be mutagenic at very high doses (Hood, 1985).

Several inorganic arsenic compounds are weak inducers of chromosomal aberrations, sister-chromatid exchange, and in vitro transformation of mammalian cells; however, there is no conclusive evidence that arsenic causes point mutations in any cellular system (Pershagen and Vahter, 1979; Belton et al., 1985; Lee et al., 1985; Deknudt et al., 1986). Studies with bacteria suggest that arsenite is a comutagen, or that it may inhibit DNA repair (Belton et al., 1985).

Arsenic is a known teratogen in several classes of vertebrates, and it has been implicated as a cause of birth defects in humans, Specific developmental malformations have been produced experimentally in mammals with inorganic As^{+3} or As^{+5} through either a single dose or a continuous dose during embryogenesis (Hanlon and Ferm, 1986b). Teratogenic effects are initiated no later than 4 hours after administration of arsenic; fetal abnormalities are primarily neural tube defects (Hanlon and Ferm, 1986c) but may also include protruding eyes, incomplete development of the skull, abnormally small jaws, and other skeletal anomalies (NRCC, 1978). Inorganic As^{+3} and As^{+5}, but not organoarsenicals, cross placental barriers in many species of mammals, which results in fetal death and malformations (NRCC, 1978; EPA, 1980). Studies with hamsters, for example, showed that sodium arsenite can induce chromatid breaks and chromatid exchanges in Chinese hamster ovary cells in a dose-dependent manner (Lee et al., 1986b). In an earlier study (Lee et al., 1986a), As^{+3} was about 10 times more potent than As^{+5} in causing transformations. The birth defects were most pronounced in golden hamsters exposed to As^{+5} during the 24-hr period of critical embryogenesis—day 8 of gestation (Ferm and Hanlon, 1985, 1986)—when 1.7 mg As^{+5}/kg body weight induced neural tube defects in about 90% of the fetuses. Hanlon and Ferm (1986a) showed that hamsters exposed to As^{+5} and heat stress (39 'C for 50 minutes) on day 8 of gestation produced a greater percentage of malformed offspring (18 to 39%) than did hamsters exposed to As^{+5} alone (4 to 8%).

6.2. Terrestrial Plants and Invertebrates

In general, arsenic availability to plants is highest in coarse-textured soils having little colloidal material and little ion exchange capacity, and lowest in fine-textured soils high in clay, organic material, iron, calcium, and phosphate (NRCC, 1978). To be absorbed by plants, arsenic compounds must be in a mobile form in the soil solution. Except for locations where arsenic content is high (e.g. around smelters), the accumulated arsenic is distributed throughout the plant

body in nontoxic amounts (NAS, 1977). For most plants, a significant depression in crop yield was evident at soil arsenic concentrations of 3 to 28 mg/L of water-soluble arsenic and 25 to 85 mg/kg of total arsenic (NRCC, 1978). Yields of peas (*Pisum sativum*), a sensitive species, were decreased at 1 mg/L of water-soluble arsenic or 25 mg/kg of total soil arsenic; rice (*Oryza sativum*) yields were decreased 75% at 50 mg/L of disodium methylarsonate in silty loam; and soybeans (*Glycine max)* grew poorly when residues exceeded 1 mg As/kg (Table 3) (NRCC, 1978). Forage plants grown in soils contaminated with up to 80 mg total As/kg from arsenical orchard sprays contained up to 5.8 mg As/kg dry weight; however, these plants were considered nonhazardous to grazing ruminants (Merry et al., 1986).

Attention was focused on inorganic arsenical pesticides after accumulations of arsenic in soils eventually became toxic to several agricultural crops, especially in former orchards and cotton fields. Once toxicity is observed, it persists for several years even if no additional arsenic treatment is made (Woolson, 1975). Poor crop growth was associated with the bioavailability of arsenic in soils. For example, alfalfa (Medicago *sativa*) and barley (*Hordeum vulgare*) grew poorly in soils containing only 3.4 to 9.5 mg As/kg, provided the soils contained excess moisture and were acidic, lightly textured, low in phosphorus and aluminum, and high in iron and calcium (Woolson, 1975). Use of inorganic arsenical herbicides, such as calcium arsenate, on golf-course turfs for control of fungal blight sometimes worsens the disease. The use of arsenicals on Kentucky bluegrass (*Poa pratensis*) is discouraged under conditions of high moisture and root stress induced by previous arsenical applications (Smiley et al., 1985).

Methylated arsenicals, as herbicides or defoliants, are sprayed on plant surfaces. They can reach the soil during application or can be washed from the plants. Additional arsenic enters soils by exchange from the roots or when dead plant materials decay (Hood, 1985). Cacodylic acid and sodium cacodylate are nonselective herbicides used in at least 82 products to eliminate weeds and grasses around trees and shrubs and to eradicate vegetation from rights-of-way and other noncrop areas (Hood, 1985). Normal application rates of various organoarsenicals for crop and noncrop purposes rarely exceed 5 kg/ha (Woolson, 1975). At recommended treatment levels, organoarsenical soil residues are not toxic to crops, and those tested (soybean, beet, wheat) were more resistant to organoarsenicals than to comparable levels of inorganic arsenicals (Woolson, 1975).

Air concentrations up to 3.9 μg As/m^3 near gold mining operations were associated with adverse effects on vegetation; higher concentrations of 19 to 69 μg As/m^3, near a coal-fired power plant in Czechoslovakia, produced measurable contamination iri soils and vegetation in a 6-km radius (NRCC, 1978).

The phytotoxic actions of inorganic and organic arsenicals are different, and each is significantly modified by physical processes. The primary mode of action of arsenite in plants is inhibition of light activation, probably through interference with the pentose phosphate pathway (Marques and Anderson, 1986). Arsenites penetrate the plant cuticle to a greater degree than arsenates (NAS,

Table 3 Lethal and Sublethal Effects of Various Arsenic Compounds on Selected Species of Terrestrial Plants and Invertebrates

Ecosystem, Organism, and Other Variables	Arsenic Concentration and Effects	Reference[a]
TERRESTRIAL PLANTS		
crops		
Total water-soluble As in soils	Depressed crop yields at 3 to 28 mg/L	1
Total soil As concentrations	Depressed crop yields at 25 to 85 mg/kg	1
Common Bermuda grass, *Cynodon dactylon*		
Arsenite	Plants grown on As-amended soils (up to 90 mg As^{+3}/kg) contained up to 17 mg As/kg dry weight (DW) in stems, 20 in leaves, and 304 in roots	2
Fruit orchards		
Inorganic arsenites and arsenates	Soils contain 31 to 94 mg As/kg DW (vs. 2.4 in untreated orchards); whole rodents contain < 0.002 mg As/kg fresh weight (FW) vs. non-detectable in untreated orchards	
Soybean, ***Glycine*** *max*		
Total As	Toxic signs at plant residues > 1 mg total As/kg	
Grasslands		
Cacodylic acid	Kill of 75 to 90% of all species at 17 kg/ha; recovery modest	
Rice, *Oryza sativum*		
Disodium methylarsonate	75% decrease in yield at soil (silty loam) concentrations of 50 mg/kg	
Scots pine, *Pinus sylvestris*		
Inorganic As^{+5}	Seedlings die when soil (sandy) concentrations exceed 250 mg/kg DW; maximum bioconcentration factors low: 0.6 for roots, 0.1 for shoots; residues > 62mg As/kg DW in shoots are toxic, and 3300 mg/kg DW usually fatal	4
Pea, *Pisum sativum*		
Sodium arsenite	15 mg/L inhibits light activation and photosynthetic CO_2 fixation in chloroplasts	5

Table *3 (Continued)*

Ecosystem, Species, and Other Variables	Arsenic Concentration and Effects	Reference[a]
Sandhill plant communities		
Cacodylic acid	No lasting effect at 2.25 kg/ha; some species defoliated at 6.8 kg/ha; significant effect, including 75% defoliation of oaks and death of all pine trees, at 34 kg/ha	3
Cowpea, *Vigna* sp.		
Total water-soluble As in soils	Decreased yields at 1 mg/L	1
Total soil As concentrations (loamy sand)	Toxic at 25 mg/kg	1
Yeast		
Arsenate	At 75 mg/L, 60% reduction in phosphate transport and glucose metabolism in 30 minutes; at 375 mg/L, 100% reduction	1
TERRESTRIAL INVERTEBRATES		
Honeybee, ***Apis*** *mellifera*		
Inorganic arsenite	Following arsenic spray dusting, dead bees contained 20.8 to 31.2 mg/kg FW (adults) or 5 to 13 mg/kg FW (larvae)	6
Beetles		
Cacodylic acid	Dietary levels of 100 to 1000 mg/kg fatal to certain pestiferous species	3
Western spruce budworm, Choristoneura occidentalis, sixth instar stage		
Arsenic trioxide	Dietary levels of 99.5 mg/kg FW ration killed 10%, 2550 mg/kg killed 50%, and 65,300 mg/kg was fatal to 90%; newly molted pupae and adults of As-exposed larvae had reduced weight, Regardless of dietary level, concentrations of As ranged up to 2640 mg/kg DW in dead pupae and 1708 mg/kg DW in adults	7

[a] 1, NRCC (197X); 2, Wang et al. (1984); 3, Hood (1985); 4, Sheppard et al (1985); 5, Marques and Anderson (1986); 6, Jenkins (1980); 7, Robertson and McLean (1985).

1977). One of the first indications of plant injury by sodium arsenite is wilting caused by loss of turgor, whereas stress due to sodium arsenate does not involve rapid loss of turgor (NAS, 1977). Organoarsenicals such as cacodylic acid enter plants mostly by absorption of sprays; uptake from the soil contributes only a minor fraction (Hood, 1985). The phytotoxicity of organoarsenical herbicides is characterized by chlorosis, cessation of growth, gradual browning, dehydration, and death (NAS, 1977). In general, plants cease to grow and develop after the roots have absorbed much arsenic (NRCC, 1978). Plants can absorb arsenic through the roots and foliage, although translocation is species dependent. Concentrations of arsenic in plants correlate highly and consistently with water-extractable soil arsenic and usually poorly with total soil arsenic (NRCC, 1978). For example, concentrations of arsenic in corn (*Zea mays*) grown in calcareous soils for 25 days were significantly correlated with the soil water-extractable arsenic fraction, but not with other fractions; extractable phosphorus was correlated positively with arsenic in corn and the water-soluble arsenic fraction (Sadiq, 1986). In the moss *Hylocomium splendens*, arsenate accumulation from solution was through living shoots, optimum uptake being between pH 3 and 5 (Wells and Richardson, 1985). Beets (Beta *vulgaris*) accumulated arsenic more readily at elevated temperatures, but the addition of phosphate fertilizers markedly depressed uptake (Merry et al., 1986).

Soils amended with arsenic-contaminated plant tissues were not measurably affected in CO, evolution and nitrification, suggesting that the effects of adding arsenic to soils do not influence the decomposition rate of plant tissues by soil microorganisms (Wang et al., 1984). The half-time of cacodylic acid is about 20 days in untreated soils and 31 days in arsenic-amended soils (Hood, 1985). Estimates of the half-time of inorganic arsenicals in soils are much longer, ranging from 6.5 years for arsenic trioxide to 16 years for lead arsenate (NRCC, 1978).

Data on arsenic effects on soil biota and insects are limited. In general, soil microorganisms are capable of tolerating and metabolizing relatively high concentrations of arsenic (Wang et al., 1984). This adaptation seems to be due to decreased permeability of the microorganism to arsenic (NAS, 1977). Tolerant soil microbiota can withstand concentrations up to 1600 mg/kg; however, growth and metabolism were reduced in sensitive species at 375 mg As/kg, and at 150 to 165 mg As/kg soils were devoid of earthworms and showed diminished quantities of bacteria and protozoans (NRCC, 1978). Honeybees (*Apis mellifera*) that were killed accidentally by sprayed As^{+3} contained 4 to 5 μg arsenic per bee (NAS, 1977), equivalent to 21 to 31 mg/kg body weight (Table 3). Larvae of the western spruce budworm (*Choristoneura occidentalis*) continued to feed on As^{+3} contaminated vegetation until a threshold level of about 2300 to 3300 mg As/kg dry weight whole larvae was reached; death then sometimes occurred (Table 3) (Robertson and McLean, 1985). Larvae that had accumulated sufficient energy reserves completed the first stage of metamorphosis but developed into pupae of subnormal weight; larvae containing $<$ 2600 mg As^{+3}/kg ultimately developed into adults of less than normal weight, and some containing $>$ 2600 mg/kg dry weight died as pupae (Robertson and McLean, 1985).

6.3. Aquatic Biota

Adverse effects of arsenicals on aquatic organisms have been reported at concentrations of 19 to 48 μg/L in water, 120 mg/kg in diets, and 1.3 to 5 mg/kg fresh weight in tissues (Table 4). The most sensitive of the aquatic species tested that showed adverse effects were three species of marine algae, which showed reduced growth in the range of 19 to 22 μg As^{+3}/L; developing embryos of the narrow-mouthed toad *(Gustrophryne curolenensis),* of which 50% were dead or malformed in 7 days at 40 μg As^{+3}/L; and a freshwater alga *(Scenedesmus obliquus),* in which growth was inhibited by 50% in 14 days at 48 μg As^{+5}/L (Table 4). Studies of mass cultures of natural phytoplankton communities chronically exposed to low levels of arsenate (1 .0 to 15.2 μg/L) showed that As^{+5} differentially inhibits certain plants, causing a marked change in species composition, succession, and predator-prey relations; the significance of these changes on carbon transfer between trophic levels is unknown (Sanders and Cibik, 1985; Sanders, 1986). Adverse biological effects have also been documented at water concentrations of 75 to 100 μg As/L. At 75 μg As^{+5}/L, growth and biomass in freshwater and marine algae were reduced; at 85 to 88 μg/L of As^{+5} or various methylated arsenicals, mortality was 10 to 32% in amphipods (*Gammarus pseudolimnaeus*) in 28 days; at 95 μg As^{+3}/L, marine red alga failed to reproduce sexually; and at 100 μg As^{+5}/L, marine copepods died, and goldfish behavior was impaired (Table 4). Rainbow trout *(Oncorhynchus mykiss)* fed diets containing up to 90 mg As^{+5}/kg were only slightly affected, but those given diets containing > 120mg As/kg (as As^{+3} or As^{+5}) grew poorly, avoided food, and failed to metabolize food efficiently; no toxic effects were reported over 8 weeks of exposure to diets containing 1600 mg/kg as methylated arsenicals (Table 4). In bluegills (*Lepomis macrochirus*), tissue residues of 1.35 mg As/kg fresh weight in juveniles and 5 mg/kg in adults are considered elevated and potentially hazardous (NRCC, 1978).

Toxic and other effects of arsenicals on aquatic life are significantly modified by numerous biological and abiotic factors (Woolson, 1975; NAS, 1977; NRCC, 1978; EPA, 1980, 1985; Howard et al., 1984; Michnowicz and Weaks, 1984; Bryant et al., 1985; Sanders, 1986). The LC_{50} values, for example, are markedly affected by water temperature, pH, Eh, organic content, phosphate concentration, suspended solids, and the presence of other substances and toxicants, as well as arsenic speciation and duration of exposure. In general, inorganic arsenicals are more toxic than organoarsenicals to aquatic biota, and trivalent species are more toxic than pentavalent species. Early life stages are most sensitive, and large interspecies differences are recorded, even among species closely related taxonomically.

Arsenic is bioaccumulated from the water by many organisms; however, there is no evidence of biomagnification in aquatic food chains (Woolson, 1975; NAS, 1977; NRCC, 1978; Hallacher et al., 1985; Hood, 1985). In a marine ecosystem based on the alga *Fucus vesiculosus,* arsenate (7.5 μg As^{+5}/L) was accumulated by all biota. After 3 months, arsenic was concentrated most efficiently by *Fucus* (120 mg/kg dry weight in apical fronds) and filamentous algal species (30 mg/kg

Table 4 Lethal and Sublethal Effects of Various Arsenic Compounds on Selected Species of Aquatic Biota

Taxonomic Group, Species, Arsenic Compound,[a] and Other Variables	Arsenic Concentration or Dose	Effect	Reference[b]
FRESHWATER PLANTS			
Algae, various species			
As^{+3}	1.7 mg/L	Toxic	1
As^{+3}	4 mg/L	Decomposition	1
As^{+3}	2.3 mg/L	95% to 100% kill of 4 species in 2 to 4 weeks	2, 3
As^{+5}	0.075 mg/L	Decreased growth	3
Alga, Ankistrodesmus *falcatus*			
As^{+5}	0.26 mg/L	Growth reduced 50% in 14 days	3
Alga, *Scenedesmus obliquus*			
As^{+5}	0.048 mg/L	Growth reduced 50% in 14 days	3
Alga, *Selenastrum capricornutum*			
As^{+5}	0.69 mg/L	Growth reduced 50% in 96 hr	3
FRESHWATER INVERTEBRATES			
Cladoceran, *Bosmina longirostris*			
As^{+5}	0.85 mg/L	50% immobilization in 96 hr	4
Cladoceran, *Daphnia magna*			
As^{+3}	0.63–1.32 mg/L	MATC[c]	3
As^{+3}	0.96 mg/L	LC_5 (28 days)	5
As^{+3}			
Starved	1.5 mg/L	50% immobilization in 96 hr	6
Fed	4.3 mg/L	50% immobilization in 96 hr	6
As^{+5}	0.52 mg/L	Reproductive impairment of 16% in 3 weeks	3
As^{+5}	0.93 mg/L	LC_5 (28 days); maximum bioconcentration factor (BCF) of 219X	5
As^{+5}	7.4 mg/L	LC_{50} in 96 hr	2
DSMA	0.83 mg/L	No deaths in 28 days	5

[a,b,c] See page 229 for footnotes.

Table 4 *(Continued)*

Taxonomic Group, Species, Arsenic Compound," and Other Variables	Arsenic Concentration or Dose	Effect	Reference"
SDMA	1.1 mg/L	No deaths in 28 days	5
Total As	1 mg/L	18% decrease in body weight in 3 weeks	1
Total As	1.4 mg/L	50% reproductive impairment in 3 weeks	1
Total As	2.8 mg/L	LC_{50} (21 days)	1
Total As	4.3-7.5 mg/L	Immobilization (21 days)	1
Cladoceran, ***Daphnia pulex***			
As^{+5}	49.6 mg/L	50% immobilization in 48 hr	4
As^{+3}	1.3 mg/L	LC_{50} in 96 hr	2, 3
As^{+3}	3 mg/L	50% immobilization in 48 hr	7
Amphipod, *Gammarus* ***pseudolimnaeus***			
As^{+3}	0.87 mg/L	50% immobilization in 96 hr	6
As^{+3}	0.088 mg/L	$LC_{,}$ (28 days)	5
As^{+3}	0.96 mg/L	LC_{100} (28 days)	5
As^{+5}	0.97 mg/L	$LC_{,}$ (28 days); no accumulations	5
DSMA	0.086 mg/L	$LC_{,}$ (28 days)	5
DSMA	0.97 mg/L	$LC_{,}$ (28 days)	5
SDMA	0.85 mg/L	LC, (28 days)	5
Snail ***Helisoma campanulata***			
As^{+3}	0.96 mg/L	$LC_{,0}$ (28 days)	5
As^{+5}	0.97 mg/L	LC, (28 days); maximum BCF of 99x.	5
DSMA	0.97 mg/L	LC, (28 days)	5
SDMA	0.085 mg/L	LC, (28 days)	5
Red crayfish, Procambarus ***clarkii***			
MSMA	Nominal concentration of 0.5 mg/L, equivalent to 0.23 mg As/L	Whole body arsenic concentration after 8-week exposure plus 8-week depuration was 0.3 mg/kg DW whole body vs. 0.4 for controls	8

Table 4 (Continued)

Taxonomic Group, Species, Arsenic Compound," and Other Variables	Arsenic Concentration or Dose	Effect	Reference"
MSMA	Nominal concentration of 5 mg/L, equivalent to 2.3 mg As/L	Exposure and depuration as above; maximum As concentration was 4.3 mg/kg DW whole body during exposure, 0.6 at end of depuration	8
MSMA	Nominal concentration of 50 mg/L, equivalent to 23.1 mg As/L	Exposure and depuration as above; maximum As concentration during exposure was 9 mg/kg DW whole animal and 2.1 at end of depuration	8
MSMA	Nominal concentration of 100 mg/L, equivalent to 46.3 mg As/L	No effect on growth or survival during 24-week exposure, but hatching success reduced to 17% vs. 78% for controls	9
MSMA	1019 mg/L	LC,, (96 hr)	9
Stonefly, ***Pteronarcys californica***			
As^{+3}	38 mg/L	LC,, (96 hr)	7
Stonefly, ***Pteronarcys dorsata***			
As^{+3}	0.96 mg/L	LC, (28 days)	5
As^{+5}	0.97 mg/L	LC,, (28 days); maximum BCF of 131x	5
DSMA	0.97 mg/L	LC, (28 days)	5
SDMA	0.85 mg/L	LC, (28 days)	5
Cladoceran, ***Simocepalus serrulatus***			
As^{+3}	0.81 mg/L	LC,, (96 hr)	3
Zooplankton			
As^{+3}	0.4 mg/L	No effect	1
As^{+3}	1.2 mg/L	Population reduction	1

Table 4 (Continued)

Taxonomic Group, Species, Arsenic Compound," and Other Variables	Arsenic Concentration or Dose	Effect	Reference*
FRESHWATER VERTEBRATEs			
Marbled salamander, ***Ambystoma opacum***			
As^{+3}	4.5 mg/L	50% mortality and malformations in 8 days in developing embryos	3
Goldfish, ***Curassius auratus***			
As^{+5}	0.1 mg/L	15% behavioral impairment in 24hr; 30% impairment in 48 hr	
As^{+3}	24.6–41.6 mg/L	$LC_{,,}$ (7 days)	1
As^{+3}	0.49 mg/L	EC_{50} (7 days)	3
MSMA	5 mg/L	$LC_{,,}$ (96 hr)	3
Narrow-mouthed toad, ***Gastrophryne carolinensis***			
As^{+3}	0.04 mg/L	50% death or malformations noted in developing embryos in 7 days	3
Channel catfish, ***Ictalurus punctatus***			
As^{+3}	25.9 mg/L	LC_{50} (96 hr)	10
Flagfish, *Jordanella floridae*			
As^{+3}	14.4 mg/L	LC_{50} (96 hr)	6
As^{+3}	2.1–4.1 mg/L	MATC	3
Bluegill, ***Lepomis macrochirus***			
As^{+3}			
Juveniles	0.69 mg/L	Reduced survival 16 weeks after a single treatment	2, 3
Adults	0.69 mg/L	Histopathology after 16 weekly treatments	2
As^{+3}	4 mg/L	Population reduction of 42% after several monthly applications	10
As^{+3}	30-35 mg/L	LC_{50} (96 hr)	7, 10
MSMA	1.9 mg/L	LC_{50} (96 hr)	3

Table 4 *(Continued)*

Taxonomic Group, Species, Arsenic Compound," and Other Variables	Arsenic Concentration or Dose	Effect	Reference"
Total As	Tissue residues of 1.35 mg/kg fresh weight in juveniles and 5 mg/kg in adults	Threshold acute toxic value	1
Spottail shiner, ***Notropis hudsonius***			
As^{+3}	45 mg/L	$LC_{,}$, (25 hr)	10
As^{+3}	29 mg/L	LC_{50} (48 hr); survivors with fin and scale damage	10
Chum salmon, ***Oncorhynchus keta***			
As^{+3}	11mg/L	$LC_{,}$, (48 hr)	10
Rainbow trout, ***Oncorhynchus****mykiss*			
As^{+3}			
Embryos	0.54 mg/L	LC_{50} (28 days)	2
Adults	23 to 26.6 mg/L	$LC_{,}$, (96 hr)	5
As^{+3}	0.96 mg/L	LC, (28 days)	7, 10
As^{+3} or As^{+5}	Fed diets containing 120 to 1600mg As/kg for 8 weeks	Growth depression, food avoidance, and impaired feed efficiency at all levels	11
As^{+5}	Fed diets containing 10 to 90mg As/kg for 16 weeks	No effect at about 10 mg/kg diet; some adaptation to dietary As observed in trout fed 90 mg/kg diet, as initial negative growth gave way to slow positive growth over time	11
As^{+5}	0.97 mg/L	LC, (28 days); no accumulations	5
DSMA	0.97 mg/L	LC, (28 days)	5
SDMA	0.85 mg/L	LC, (28 days)	5
SC	1000 mg/L	LC, (28 days)	12

Table *4* ***(Continued)***

Taxonomic Group, Species, Arsenic Compound," and Other Variables	Arsenic Concentration or Dose	Effect	Reference*
DMA or ABA	Fed diet containing 120 to 1600 mg/kg for 8 weeks	No toxic response at any level tested	11
Minnow, *Phoxinus* ***phoxinus***			
As^{+3}	20 mg/L	Equilibrium loss in 36 hr	10
As^{+5}	2344250 mg/L	Lethal	10
Fathead minnow, ***Pimephales****promelas*			
As^{+3}	14.1 mg/L	$LC_{,,}$ (96 hr)	6
As^{+3}	2.1–4.8 mg/L	MATC[c]	6
As^{+5}	25.6 mg/L	$LC_{,,}$ (96 hr)	3
As^{+5}	0.53–1 SO mg/I	MATC[c]	3
Brook trout, *Salvelinus fontinalis*			
As^{+3}	1.5 mg/L	LC_{50} (96 hr)	3
MARINE PLANTS			
Algae, 2 spp.			
As^{+3} or As^{+5}	1 mg/L	No effect	13
As^{+5}	1000 mg/L	No deaths	13
Algae, 3 spp.			
As^{+3}	0.019–0.022 mg/L	Reduced growth	3
Red alga, ***Champia*** *parvula*			
As^{+3}	0.065 mg/L	Normal sexual reproduction	13
As^{+3}	0.095 mg/L	Normal sexual reproduction	13
As^{+3}	0.30 mg/L	Death	13
As^{+5}	10 mg/L	Normal growth but no sexual reproduction	13
Phytoplankton			
As^{+5}	0.075 mg/L	Reduced biomass of populations in 4 days	4
Red Alga, *Plumaria* ***elegans***			
As^{+3}	0.58 mg/L	Arrested sporeling development 7 days after exposure for 18 hr	2

Table 4 *(Continued)*

Taxonomic Group, Species, Arsenic Compound,[a] and Other Variables	Arsenic Concentration or Dose	Effect	Reference*
Alga, ***Skeletonema*** costatum			
As^{+5}	0.13 mg/L	Growth inhibition	3
Alga, ***Thalassiosira aestivalis***			
As^{+5}	0.075 mg/L	Reduced chlorophyll a	3
MARINE INVERTEBRATES			
Copepod, ***Acartia clausi***			
As^{+3}	0.5 1 mg/L	$LC_{,,}$ (96 hr)	3
Dungeness crab, ***Cancer*** magister			
As^{+5}	0.23 mg/L	$LC_{,,}$ (96 hr) for zoea	3
Amphipod, ***Corophium volutator***			
As^{+5}			
Water temperature. °C			
5	8 mg/L	$LC_{,,}$ (230 hr)	14
10	8 mg/L	$LC_{,,}$ (150 hr)	14
15	8 mg/L	$LC_{,,}$ (74 hr)	14
15	4 mg/L	$LC_{,,}$ (140 hr)	14
15	2 mg/L	$LC_{,,}$ (192 hr)	14
Pacific oyster, ***Crassostrea gigas***			
As^{+3}	0.33 mg/L	$LC_{,,}$ (96 hr) for embryos	3
American oyster, ***Crassostrea virginica***			
As^{+3}	7.5 mg/L	LC_{50} (48 hr, eggs)	10
Copepod, ***Eurytemora affinis***			
As^{+5}	0.025 mg/L	No effect	15
As^{+5}	0.1 mg/L	Reduced juvenile survival	15
As^{+5}	1 mg/L	Reduced adult survival	15
Clam, *Macoma* balthica			
As^{+5}			
Water temperature, °C			
5	220 mg/L	$LC_{,,}$ (192 hr)	14
10	60 mg/L	$LC_{,,}$ (192 hr)	14
15	15 mg/L	$LC_{,,}$ (192 hr)	14
Mysid, ***Mysidopsis bahia***			
As^{+3}	0.63 – 1.27 mg/L	MATC[c]	3
As^{+5}	2.3 mg/L	$LC_{,,}$ (96 hr)	3
Blue mussel, Mytilus ***edulis***			
As^{+3}	16 mg/L	Lethal in 3 to 16 days	10

Table 4 (Continued)

Taxonomic Group, Species, Arsenic Compound,[a] and Other Variables	Arsenic Concentration or Dose	Effect	Reference[b]
Mud snail, *Nassarius obsoletus*			
As^{+3}	2 mg/L	Depressed oxygen consumption in 72 hr	10
Oligochaete annelid, *Tubifex costatus*			
As^{+5}			
Water temperature, °C			
5	500 mg/L	$LC_{,,}$ (I 30 hr)	14
10	500 mg/L	$LC_{,,}$ (1 1.5 hr)	14
15	500 mg/L	$LC_{,,}$ (85 hr)	14
MARINE VERTEBRATES			
Grey mullet, *Chelon labrosus*			
As^{+3}	27.3 mg/L	$LC_{,,}$ (96 hr); some skin discoloration	16
Dab, ***Limanda limanda***			
As^{+3}	8.5 mg/L	$LC_{,,}$ (96 hr); respiratory problems	16
Pink salmon, ***Oncorhynchus gorbuschu***			
As^{+3}	2.5 mg/L	LC, (10 days)	10
As^{+3}	3.8 mg/L	LC_{54} (10 days)	3
As^{+3}	7.2 mg/L	LC_{100} (7 days)	3
Teleosts, 3 spp.			
As^{+3}	12.7–16 mg/L	$LC_{,,}$ (96 hr)	3

[a] As^{+3}, inorganic trivalent arsenite; As^{+5}, inorganic pentavalent arsenate; DMA, dimethylarsinic acid; ABA, p-aminobenzenearsonic acid; DSMA, disodium methylarsenate [$CH_3AsO(ONa)_2$]; SDMA, sodium dimethylarsenate [$(CH_3)_2AsO(ONa)$]; MSMA, monosodium methanearsonate; SC, sodium cacodylate.

[b] 1,NRCC (1978); 2,EPA (1980); 3,EPA (1985); 4, Passino and Novak (1984); 5,Speharet al. (1980); 6,Lima et al. (1984); 7, Johnson and Finley, (1980); 8,Naqvi et al. (1990); 9,Naqvi and Flagge (1990); 10, NAS (1977); 11, Cockell and Hilton (1985); 12, Hood (1985); 13,Thursby and Steele (1984); 14,Bryant et al. (1985); 15, Sanders (1986); 16, Taylor et al. (1985).

[c] Maximum acceptable toxicant concentration. Lower value in each pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, or metabolism during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

dry weight); there was little or no bioaccumulation in mussels (Rosemarin et al., 1985). In a freshwater food chain composed of algae, daphnids, and fish, water concentrations of 0.1 mg cacodylic acid/L produced residues after 48 hr of 4.5 (mg As/kg dry weight) in algae and 3.9 in daphnids, but only 0.09 in fish (NAS, 1977). Microcosms of a Delaware cordgrass (*Spartina alterniflora*) salt marsh exposed to

elevated levels of As^{+5} showed that virtually all arsenic was incorporated into plant tissue or strongly sorbed to cell surfaces (Sanders and Osman, 1985). Studies with radioarsenic and mussels (*Mytilus galloprovincialis*) showed that accumulation varied with nominal arsenic concentration, tissue, age of the mussel, and temperature and salinity of the medium (Unlu and Fowler, 1979). Arsenate uptake increased with increasing arsenic concentration in the medium, but the response was not linear, accumulation being suppressed at higher external arsenic concentrations. Smaller mussels took up more arsenic than larger ones. In both size groups, arsenic was concentrated in the byssus and digestive gland. In general, arsenic uptake and loss increased at increasing temperatures. Uptake was significantly higher at 1.9% salinity than at 3.8%, but the loss rate was about the **same** at both salinities. Radioarsenic loss followed a biphasic pattern; biological half-life was 3 and 32 days for the fast and slow compartments, respectively; secretion via the byssal thread played a key role in elimination (Unly and Fowler, 1979). Factors known to modify rates of arsenic accumulation and retention in a marine shrimp (*Lysmata seticaudata*) include water temperature and salinity, arsenic concentration, age, and especially frequency of molting (Fowler and Unlu, 1978).

Bioconcentration factors (BCF) experimentally determined for arsenic in aquatic organisms are, except for algae, relatively low. The BCF values for inorganic As^{+3} in most aquatic invertebrates and fish exposed for 21 to 30 days did not exceed 17 times; the maxima were 6 times for As^{+5} and 9 times for organoarsenicals (EPA, 1980, 1985). Significantly higher BCF values were recorded in other aquatic organisms (NRCC, 1978), but they were based on mean arsenic concentrations in natural waters that seemed artificially high. A BCF of 350 times was reported for the American oyster (*Crassostrea uirginica)* held in 5 $\mu g\ As^{+5}/L$ for 112 days (Zaroogian and Hoffman, 1982). There was no relation between oyster body burden of arsenic and exposure concentration; however, diet seemed to contribute more to arsenic uptake than did seawater concentration (Zaroogian and Hoffman, 1982). An arsenic-tolerant strain of freshwater alga (*Chlorella vulgarus*) from an arsenic-polluted environment showed increasing growth up to 2000 mg As^{+5}/L, and it could survive at 10,000 mg As^{+5}/L (Maeda et al., 1985). Accumulations up to 50,000 mg As/kg dry weight were recorded (Maeda et al., 1985), suggesting a need for additional research on the extent of this phenomenon and its implications on food-web dynamics.

Some investigators have suggested that arsenic in the form of arsenite is preferentially utilized by marine algae and bacteria (Johnson, 1972; Bottino et al., 1978; Johnson and Burke, 1978). Arsenate reduction to arsenite in seawater depends on phosphorus in solution and available algal biomass (Johnson and Burke, 1978). During algal growth, as phosphate is depleted and the P^{+5}: As^{+5} ratio drops, the rate of As^{+5} reduction increases. The resultant As^{+3}, after an initial peak, is rapidly oxidized to As^{+5}, indicating the possibility of biological catalysis as well as mediation of As^{+5} reduction. Researchers generally agree that As^{+3} is more toxic than arsenates to higher organisms; however, As^{+5} has a more profound effect on the growth and morphology of marine algae than does As^{+3}.

Possibly, marine algae erect a barrier against the absorption of As^{+3} but not against As^{+5}. Within the cell, As^{+5} can then be reduced to the possibly more toxic As^{+3}. For example, the culture of two species of marine algae (*Tetraselmis chui, Hymenomonas carterue)* in media containing various concentrations of As^{+5} or As^{+3} showed that arsenic effects varied with oxidation state, concentration, and light intensity. Arsenate was incorporated and later partly released by both species. Differences between rates of uptake and release suggest that arsenic undergoes chemical changes after incorporation into algal cells (Bottino et al., 1978). When bacterial cultures from the Sargasso Sea and from marine waters off of Rhode Island were grown in As^{+3}-enriched media, the bacteria reduced all available As^{+5} and utilized As^{+3} during the exponential growth phase, presumably as an essential trace nutrient. The arsenate reduction rate per cell was estimated to be 75 x 10^{-11} mg As/minute (Johnson, 1972).

The ability of marine phytoplankton to accumulate high concentrations of inorganic arsenicals and to transform them into methylated arsenicals that are later effeciently transferred in the food chain is well documented (Irgolic et al., 1977; Benson, 1984; Matsuto et al., 1984; Freeman, 1985; Froelich et al., 1985; Maeda et al., 1985; Norin et al., 1985; Sanders, 1985; Yamaoka and Takimura, 1986). Algae constitute an important source of organoarsenic compounds in marine food webs. In the food chain composed of the alga *Dunuliellu marina,* the grazing shrimp *Artemia salina*, and the carnivorous shrimp *Lysmata seticaudata*, organic forms of arsenic were derived from in vivo synthesis by *Dunuliellu* and efficiently transferred, without magnification, along the food chain (Wrench et al., 1979). Laboratory studies with five species of euryhaline algae grown in freshwater or seawater showed that all species synthesized fat-soluble and water-soluble arsenoorganic compounds from inorganic As^{+3} and As^{+5}. The BCF values in the five species ranged from 200 times to about 3000 times--accumulations being highest in lipid phases (Lunde, 1973). In Charlotte Harbor, Florida, a region that has become phosphate-enriched due to agricultural activity, virtually all of the arsenic taken up by phytoplankton was biomethylated and returned to the estuary, usually as monomethylarsonic and dimethylarsenic acids (Froelich et al., 1985). The ability of marine phytoplankton to methylate arsenic and release the products to the surrounding environment varies between species, and even within a particular species, according to their possession of the necessary methylating enzymes (Sanders, 1985). The processes involved in detoxifying arsenate after its absorption by phytoplankton are not firmly established but seem to be nearly identical in all plants, suggesting a similar evolutionary development. Like phosphates and sulfates, arsenate may be fixed with ADP, reduced to the arsonous level, and successfully methylated and adenosylated, ultimately producing the 5-dimethylarsenosoribosyl derivatives accumulating in algae (Benson, 1984).

Sodium arsenite has been used extensively as an herbicide for the control of mixed submerged aquatic vegetation in freshwater ponds and lakes; concentrations of 1.5 to 3.8 mg As^{+3}/L have usually been effective and are considered safe for fish (NAS, 1977). However, As^{+3} concentrations considered effective for

aquatic weed control may be harmful to several species of freshwater teleosts, including bluegills, flagfish (*Jordanella floridae*), fathead minnows (*Pimephales promelas*), and rainbow trout (*Oncorhynchus mykiss*) (Table 4). Fish exposed to 1 to 2 mg total As/L for 2 to 3 days may show one or more of several signs: hemorrhagic spheres on gills, fatty infiltration of the liver, and necrosis of heart, liver, and ovarian tissues (NRCC, 1978). In green sunfish *(Lepomis cyanellus)*, hepatocyte changes parallel arsenic accumulation in the liver (Sorensen et al., 1985). Organoarsenicals are usually eliminated rapidly by fish and other aquatic fauna. Rainbow trout, for example, fed a marine diet containing 15 mg organic As/kg had only negligible tissue residues 6 to 10 days later, although some enrichment was noted in the eyes, throat, gills, and pyloric caeca (Pershagen and Vahter, 1979). Oral administration of sodium arsenate to estuary catfish (*Cnidoglanis macrocephalus*) and school whiting (*Sillago bassensis*) resulted in tissue accumulations of trimethylarsine oxide. Arsenobetaine levels, which occur naturally in these teleosts, were not affected by As^{+5} dosing. The toxicity of trimethylarsine oxide is unknown, but the ease with which it can be reduced to the highly toxic trimethylarsine is cause for concern (Edmonds and Francesconi, 1987).

6.4. Birds

Signs of inorganic trivalent arsenite poisoning in birds (muscular incoordination, debility, slowness, jerkiness, falling, hyperactivity, fluffed feathers, drooped eyelids, huddled position, unkempt appearance, loss of righting reflex, immobility, seizures) were similar to those induced by many other toxicants and did not seem to be specific for arsenosis. Signs occurred within 1 hr and death within 1 to 6 days after administration; remission took up to 1 month (Hudson et al., 1984). Internal examination suggested that the lethal effects of acute inorganic arsenic poisoning were due to the destruction of blood vessels lining the gut, which resulted in decreased blood pressure and subsequent shock (Nyström, 1984). For example, coturnix *(Coturnix coturnix)* exposed to acute oral doses of As^{+3} showed hepatocyte damage (swelling of granular endoplasmic reticulum); these effects were attributed to osmotic imbalance, possibly induced by direct inhibition of the sodium pump by arsenic (Nyström, 1984).

Arsenic, as arsenate, in aquatic plants (up to 430 mg As/kg plant dry weight) from agricultural drainwater areas can impair normal development of mallard ducklings (Camardese et al., 1990) (Table 5). Pen studies with ducklings showed that diets of 30mg As/kg ration adversely affects growth and physiology, and 300mg As/kg diet alters brain biochemistry and nesting behavior. Decreased energy levels and altered behavior can further decrease duckling survival in a natural environment (Camardese et al., 1990).

Western grasshoppers (*Melanophis* spp.) poisoned by arsenic trioxide were fed, with essentially no deleterious effects, to nestling northern bobwhites (*Colinus virginianus),* mockingbirds (*Mimus polyglottos*), American robins (*Turdus migratorius*), and other songbirds (NAS, 1977). Up to 134 poisoned grasshoppers, containing a total of about 40 mg arsenic, were fed to individual nestlings without any apparent toxic effect. Species tested that were most sensitive to various arsenicals

Table 5 Lethal and Sublethal Effects of Various Arsenicals on Selected Species of Birds

Species and Arsenic Compound	Effect	Reference[a]
Chukar, ***Alectoris chukar***		
Silvisar-510 (mixture of cacodylic acid and triethanolamine cacodylate)	Single oral LD_{50} dose of about 2000 mg/kg body weight (BW); signs of poisoning evident within 10 minutes and mortalities within 1 to 2 days; remission took up to one month	1
Mallard, *Anas platyrhynchos*		
Sodium arsenate	Ducklings were fed 30,100, or 300 mg As/kg diet for 10 weeks. All treatment levels produced elevated hepatic glutathione and ATP concentrations and decreased overall weight gain and rate of growth in females. Arsenic concentrations were elevated in brain and liver of ducklings fed 100 or 300 mg/kg diets; at 300 mg/kg, all ducklings had altered behavior, i.e., increased resting time; male ducklings had reduced growth	2
Sodium arsenite	323 mg/kg BW is LD_{50}, acute oral value	1, 3, 4
Sodium arsenite	500 mg/kg diet is fatal to 50% in 32 days; 1000 mg/kg diet fatal to 50% in 6 days	3
Sodium cacodylate	1740 to 5000 mg/kg diet not measurably harmful to ducklings in 5 days	5
Silvisar 510	Single oral LD_{50}, > 2400 mg/kg BW; regurgitation and excessive drinking noted	1
Lead arsenate	5000 mg/kg diet not fatal in 11 days	3
Copper acetoarsenite	5000 mg/kg diet fatal to 20% in 11 days	3
California quail, *Callipepla californica*		
Sodium arsenite	Single oral LD_{50} value of 47.6 mg/kg BW	1
Northern bobwhite, Colinus *virginianus*		
Copper acetoarsenite	480 mg/kg in diet fatal to 50% in 11 days	3
Sodium cacodylate	1740 mg/kg in diet for 5 days produced no effect on behavior, no signs of intoxication, and negative necropsy	5

Table 5 ***(Continued)***

Species and Arsenic Compound	Effect	Reference[a]
Monosodium methanearsonate, CH_4AsNaO_3	Single oral LD_{50} dose of 3300 mg/kg BW	5
Chicken, *Gallus gallus*		
Inorganic trivalent arsenite	Up to 34% dead embryos at dose range of 0.01 – 1 $\mu g\ As^{+3}$/embryo; threshold for malformations at dose range 0.03–0.3 μg/embryo	4
Inorganic pentavalent arsenate	Up to 8% dead at dose range 0.01 – 1 $\mu g\ As^{+5}$/embryo; threshold for malformations at dose range 0.3-3 μg/embryo	4
Disodium methylarsenate	Teratogenic to embryos when injected at 1 to 2 mg/egg	4, 5
Sodium cacodylate	Developmental abnormalities at embryonic injected doses of 1 to 2 mg/egg	5
Dodecylamine p-chlorophenylarsonate	At dietary levels of 23.3 mg/kg, liver residues were 2.9 mg/kg fresh weight (FW) at 9 weeks. No ill effects noted	6
3-Nitro-4-hydroxy-phenylarsonic acid	At 18.7 mg/kg diet for 9 weeks, liver residues of 2.4 mg/kg FW. Those fed diets containing 187 mg/kg for 9 weeks had no ill effects; liver content of 7.5 mg/kg FW	6
3-Nitro-4-hydroxy-phenylarsonic acid	LD_{50} dose of 33 mg/kg BW (single oral) or 9.7 mg/kg BW (intraperitoneal injection)	3
Arsanilic acid	Fed diets containing 45 mg/kg for 9 weeks; no effect except slightly elevated liver content of 1.2 mg/kg FW. At dietary levels of 455 mg/kg, liver residues were 6.4 mg/kg FW after 9 weeks; no other effects evident	6
Cacodylic acid	Dosed orally without effect at 100 mg/kg BW daily for 10 days	5
Chickens, *Gallus* spp.		
Arsanilic acid	50% excreted in 36 to 38 hr	4
Arsenate	50% excreted in 60 to 63 hr	4
Turkey, ***Meleagris gallopavo***		
3-Nitro-4-hydroxy-phenylarsonic acid	Single oral LD_{50} dose of 17.4 mg/kg BW	3
Brown-headed cowbird, ***Molothrus ater***		
Copper acetoarsenite	All survived 11 mg/kg diet for 6	

Table 5 *(Continued)*

Species and Arsenic Compound	Effect	Reference[a]
	months; maximum whole body residue of 1.7 mg As/kg dry weight (DW)	3
Copper acetoarsenite	All survived 33 mg/kg diet for 6 months (whole body content of 6.6 mg As/kg DW) or 7 months (8.6 DW)	3
Copper acetoarsenite	*99.8* mg/kg in diet fatal to 50% in 11 days	3
Copper acetoarsenite	100 mg/kg in diet for 3 months fatal to 100%; tissue residues, in mg/kg DW, of 6.1 in brain, 40.6 in liver	3
Gray partridge, ***Perdix perdix***		
Lead arsenate	300 mg/kg BW fatal in 52 hr	3
Ring-necked pheasant, ***Phasianus colchicus***		
Sodium arsenite	Single oral dose of 386 mg/kg BW is $LD_{,,}$ value	1
Copper acetoarsenite	Single oral dose of 1403 mg/kg BW is $LD_{,,}$ value	4
Lead arsenate	*4989* mg/kg in diet fatal	3

[a] 1, Hudson et al., 1984; 2, Camardese et al., 1990; 3, NAS, 1977; 4, NRCC, 1978; 5, Hood, 1985; 6, Woolson, 1975.

were the brown-headed cowbird (*Molothrus ater*), with an $LD_{,,}$ (1 l-day) value of 99.8 mg of copper acetoarsenite/kg diet; California quail (*Callipepla californica*), with an $LD_{,,}$ single oral dose value of 47.6 mg of sodium arsenite/kg body weight; and chicken with 33 and turkey with 17.4 mg/kg body weight of 3-nitro-4-hydroxyphenylarsonic acid as a single oral $LD_{,,}$ dose (Table 5).

Chickens rapidly excrete arsenicals; only 2% of dietary sodium arsenite remained after 60 hr (NAS, 1977), and arsanilic acid was excreted largely unchanged (Woolson, 1975). Excretion of arsanilic acid by chickens was affected by uptake route: excretion was more rapid when administration was by intramuscular injection than when it was oral (NRCC, 1978). Studies with inorganic As^{+5} and chickens indicated that (1) arsenates rapidly penetrated the mucosal and serosal surfaces of epithelial membranes, (2) As^{+5} intestinal absorption was essentially complete within 1 hr at 370mg As^{+5}/kg body weight but only 50% complete at 3700 mg/kg body weight, (3) vitamin D_3 was effective in enhancing duodenal As^{+5} absorption in rachitic chicks, and (4) As^{+5} and phosphate did not appear to share a common transport pathway in the avian duodenum (Fullmer and Wasserman, 1985).

6.5. Mammals

Mammals are exposed to arsenic primarily through the ingestion of naturally contaminated vegetation and water or through human activity. In addition, feed additives containing arsonic acid derivatives are often fed to domestic livestock to promote growth and retard disease. Some commercial pet foods contain up to 2.3 mg As/kg dry weight (NRCC, 1978). Uptake may occur by ingestion (the most likely route), inhalation, or absorption through skin and mucous membranes. Soluble arsenicals are absorbed more rapidly and completely than the sparingly soluble arsenicals, regardless of the route of administration (NRCC, 1978).

Acute episodes of poisoning in warm-blooded organisms by inorganic and organic arsenicals are usually characterized by high mortality and morbidity over a period of 2 to 3 days (NAS, 1977; Selby et al., 1977). General signs of arsenic toxicosis include intense abdominal pain, staggering gait, extreme weakness, trembling, salivation, vomiting, diarrhea, fast and feeble pulse, prostration, collapse, and death. Gross necropsy shows a reddening of gastric mucosa and intestinal mucosa, a soft yellow liver, and red edematous lungs. Histopathological findings show edema of gastrointestinal mucosa and submucosa, necrosis and sloughing of mucosal epithelium, renal tubular degeneration, hepatic fatty changes and necrosis, and capillary degeneration in the gastrointestinal tract, vascular beds, skin, and other organs. In subacute episodes, in which animals remain alive for several days, signs of arsenosis include depression, anorexia, increased urination, dehydration, thirst, partial paralysis of the rear limbs, trembling, stupor, coldness of extremities, and subnormal body temperatures (NAS, 1577; Selby et al., 1977). In cases involving cutaneous exposure to arsenicals, a dry, cracked, leathery, and peeling skin may be a prominent feature (Selby et al., 1977). Nasal discharges and eye irritation were documented in rodents exposed to organoarsenicals in inhalation toxicity tests (Hood, 1985). Subacute effects in humans and laboratory animals include peripheral nervous disturbances, melanosis, anemia, leukopenia, cardiac abnormalities, and liver changes. Most adverse signs rapidly disappear after exposure ceases (Pershagen and Vahter, 1979).

Arsenic poisoning in most animals is usually manifested by acute or subacute signs; chronic poisoning is infrequently seen (NAS, 1977). The probability of chronic arsenic poisoning from continuous ingestion of small doses is rare because detoxication and excretion are rapid (Woolson, 1975). Chronic toxicity of inorganic arsenicals is associated with weakness, paralysis, conjunctivitis, dermatitis, decreased growth, and liver damage (NRCC, 1978). Arsenosis, produced as a result of chronic exposure to organic arsenicals, is associated with demyelination of the optic and sciatic nerves, depressed growth, and decreased resistance to infection (NRCC, 1978).

Research results on arsenic poisoning in mammals (Table 6) show general agreement on eight points: (1) arsenic metabolism and effects are significantly influenced by the organism tested, the route of administration, the physical and chemical form of the arsenical, and the dose; (2) inorganic arsenic compounds are

Table 6 Lethal and Sublethal Effects of Various Arsenicals on Selected Species of Mammals

Organism and Arsenical	Effect	Reference"
Cow, Bos hovis		
Arsenate	Cows fed 33 mg As^{+5} daily per animal for 3 months had slightly elevated levels in muscle CO.02 mg/kg fresh weight (FW) vs. 0.005 in controls] and liver (0.03 vs. 0.012) but normal levels in milk and kidney	
Arsenite	Cows fed 33 mg As^{+3} daily per animal for 15 to 28 months had tissue levels, in mg/kg FW, of 0.002 for milk (vs. < 0.001 for controls), 0.03 for muscle (vs. 0.005), 0.1 for liver (vs. 0.012), and 0.16 for kidney (vs. ***0.053)***	
Cattle, *Bos* spp.		
Arsenic pentoxide (Wood ashes treated with As preservative)	Several deaths after eating wood ashes (780 mg/kg dry weight); tissue residues, in mg As/kg FW, of 13.9 in liver, 23.7 in kidney, and 25.8 in rumen contents (vs. control values of < 0.5)	*2*
Arsenic trioxide	Single oral dose of 15 to 45 g/ animal was fatal	*3*
Arsenic trioxide	Toxic dose is 33 to 55 mg/kg body weight (BW), or 13.2 to 22 g for a 400-kg animal. Animals accidentally poisoned topically contained up to 15 mg As/kg FW liver, 23 in kidney, and 45 in urine (vs. < 1 for all control tissues)	*4*
Cacodylic acid, $(CH_3)_2AsO(OH)$	Calves were anorexic in 3 to 6 days when fed diets containing 4700 mg/kg. Adult oral dosages of 10 mg/kg BW daily for 3 weeks followed by 20 mg/kg BW daily for 5 to 6 weeks were lethal. Adverse effects at 25 mg/kg BW daily for 10 days	5
Methanearsonic acid, $CH_3AsO(OH)_2$	Calves were anorexic in 3 to 6 days when fed diets containing 4000 mg/kg	5
Monosodium methanearsonate	10 mg/kg BW daily for 10 days was fatal	3
Sodium arsenite	Single oral dose of 1 to 4g was fatal	3
Dog, ***Canis familiaris***		
Cacodylic acid	Single oral $LD_{,,}$ value of 1000 mg/kg BW. Fed diets containing 30 mg/kg for 90 days with no ill effects	5
Methanearsonic acid	Fed diets containing 30 mg/kg for 90 days with no ill effects	5
Sodium arsenite	50 to 150 mg was fatal	3

Table 6 *(Continued)*

Organism and Arsenical	Effect	Reference[a]
Domestic goat, Capra sp.		
Arsenic acid	Single oral dose of 2.5 to 7.5 mg/kg BW (50 to 150 mg) was acutely toxic	3
Guinea pig, ***Cavia*** sp.		
Arsanilic acid	Dietary levels of 350 mg/kg resulted in blindness and optic disc atrophy in 25 to 30 days	6
Arsenic trioxide	Fed diets containing 50 mg/kg for 21 days; elevated As residues, in mg/kg FW, of 4 in blood, 15 in spleen, and 20 in heart (vs. <1 for all control tissues)	7
Sodium arsanilate	Subcutaneous injection of 70 mg/kg BW caused degeneration of sensory walls of inner ear; elevated As residues in cochlea	6
Sodium arsenate	Intraperitoneal injection of 0.2 mg/kg BW at age 2 months caused deafness	6
Hamster, ***Cricetus sp.***		
Arsenate	Maternal dose of 5 mg As $^{+5}$/kg BW caused some fetal mortality, but no malformations; higher dose of 20 mg/kg BW caused 54% fetal deaths and malformations	3
Calcium arsenate	Pulmonary tumorogenicity demonstrated 70 weeks after 15 intratracheal weekly injections of 3 mg/kg BW	8
Dimethylarsinate	50% growth reduction in Chinese hamster ovary cells (CHOC) at 90 to 112 mg/L	9
Gallium arsenide	Single oral dose of 100 mg/kg BW mostly (85%) eliminated in 5 days, usually in form of organoarsenicals; all tissue levels < 0.25 mg/kg	10
Sodium arsenate	Dosed intravenously on day 8 of gestation: 2 mg/kg BW had no measurable effect; 8 mg/kg BW produced increased incidence of malformation and resorption; 16 mg/kg BW killed all embryos.	6
Sodium arsenate	50% growth reduction in CHOC at 2.25 mg/L	9
Sodium arsenite	Chinese hamster ovary cells showed 50% growth reduction at 0.3 mg/L	9
Sodium cacodylate	Single intraperitoneal injection of 900 to 1000 mg/kg BW during midgestation resulted in some maternal deaths and increased incidence of fetal malformations	5
Horse, *Equus caballus*		
Sodium arsenite	Daily doses of 2 to 6 mg/kg BW (1 to 3 g) for 14 weeks were fatal	3

Table 6 (*Continued)*

Organism and Arsenical	Effect	Reference"
Cat, *Felis domesticus*		
Inorganic arsenate or arsenite	Chronic oral toxicity at 1.5 mg/kg BW	6
Human, ***Homo sapiens***		
Arsenic trioxide	Fatal at 70 to 180 mg, equivalent to about 1 to 2.6 mg As/kg BW	6
Arsenic trioxide	LD,, dose of 7 mg/kg BW	3
Cacodylic acid	LD,, of 1,350 mg/kg BW	3
Lead arsenate	Some deaths at 7 mg/kg BW	3
Total arsenic	Accumulations of 1 mg/kg BW daily for 3 months in children, or 80 mg/kg BW daily for 3 years, produced symptoms of chronic arsenic poisoning	3
Total arsenic, daily oral dose	Prolonged dosages of 3 to 4mg daily produced clinical symptoms of chronic arsenic intoxication	3
Total arsenic in drinking and cooking water	Prolonged use produced symptoms of chronic arsenic intoxication (0.6 mg/L) or skin cancer (0.29 mg/L)	3
Total arsenic , probably as arsenate	12,000 Japanese infants poisoned (128 deaths) from consumption of dry milk contaminated with arsenic; average exposure of 3.5 mg *As* daily for one month. Severe hearing loss, brain-wave abnormalities, and other central nervous system disturbances noted 15 years after exposure	6
Total inorganic arsenic	Daily dose of 3 mg for 2 weeks may cause severe poisoning in infants and symptoms of toxicity in adults	6
Cynomolgus monkey, *Macaca* sp.		
Fish arsenic meal (witch flounder, ***Glyptocephalus cynoglossus)*** containing 77 mg total As/kg	Given single meal at 1 mg/kg BW; tissue residues normal after 14 days	11
As above, except arsenic trioxide substituted for total arsenic	As above	11
Mammals, many species		
Calcium arsenate	Single oral LD,, range of 35 to 100 mg/kg BW	3
Lead arsenate	Single oral LD,, range of 10 to 50 mg/kg BW	3

Table *6 (Continued)*

Organism and Arsenical	Effect	Reference"
Mammals, most species		
Arsenic trioxide	3 to 250 mg/kg BW lethal	12
Sodium arsenite	1 to 25 mg/kg BW lethal	12
Mouse, *Mus* spp.		
Arsenate	Maternal dose of 10 mg As^{+5}/kg BW resulted in some fetal deaths and malformations	3
Arsenic trioxide	Single oral $LD_{,,}$ (96 hr) value of 39.4 mg/kg BW; LD, (96 hr) of 10.4 mg/kg BW	12
Arsenic trioxide	"Adapted' group (50 mg As/L in drinking water for 3 months) had subcutaneous $LD_{,,}$ value of 14 mg/kg BW vs. 11 for nonadapted group	12
Arsenic trioxide	Air concentrations of 28.5 mg/m^3 for 4 hr daily on days 9 to 12 of gestation caused fetotoxic effects and chromosomal damage to liver cells by day 18; effects included reduced survival, impaired growth, retarded limb ossification, and bone abnormalities. At 2.9 mg/m^3, a 9.9% decrease in fetal weight was recorded; at 0.26 mg/m^3, a 3.1% decrease was measured	13
Cacodylic acid	Oral dosages of 400 to 600 mg/kg BW on days 7 to 16 of gestation produced fetal malformations (cleft palate), delayed skeletal ossification, and reduced fetal weight	5
Sodium arsenate	Maximum tolerated doses in terms of abortion or maternal death over 24 hr in 18-day pregnant mice were 20mg As^{+5}/kg BW, intraperitoneal route, and 50 mg/kg BW administered orally. Residue half-life was about 10 hr regardless of route of administration	14
Sodium arsenite	Fed 5 mg/kg diet for three generations: reduced litter size, but outwardly normal	6
Sodium arsenite	$LD_{,,}$ of 9.6 mg/kg BW, subcutaneous route; $LD_{,,}$ (7 days after administration) of 11.3 mg/kg BW, subcutaneous route	15
Sodium arsenite	$LD_{,,}$ of 12 mg/kg BW, intraperitoneal route. At 10 mg/kg BW, damage to bone marrow and sperm	16
Sodium cacodylate	Single intraperitoneal injection of 1200 mg/kg BW during midgestation	

Table 6 (Continued)

Organism and Arsenical	Effect	Reference"
	resulted in increased rates of fetal skeletal malformations	5
Mule deer, ***Odocoileus hemionushemionus***		
Silvisar-510 (mixture of cacodylic acid and triethanolamine cacodylate)	Single oral $LD_{,,}$ dose > 320 mg/kg BW produced appetite loss	17
White-tailed deer, Odocoileus ***virqinianus***		
Sodium arsenite (used to debark trees)	Lethal dose of 923 to 2770 mg, equivalent to about 34 mg/kg BW; liver residues of 40 mg/kg FW	12
Arsenic acid (herbicide to control Johnson grass)	23 deer killed from apparent misuse. Arsenic levels, in mg/kg FW, in deer found dead were 19 in liver, 18 in kidney, and 22.5 in rumen contents. Soils from area contained about 2.4 mg As/kg; water contained 0.42 mg As/L	12
Domestic sheep, Ovis *aries*		
Arsanilic acid	One-year-old castrates fed diets with 273 mg As/kg for 28 days had 0.54 mg As/L in blood, 29 mg/kg DW in liver, 24 in kidney, and 1.2 in muscle (vs. < 0.01 in all control tissues). After 6 days on an As-free diet, liver residues were < 5 mg/kg DW. Maximum tissue levels in sheep fed diets containing 27 mg As/kg for 28 days was 3.2 mg/kg DW kidney; for an 144 mg/kg diet, the maximum tissue level was 27 mg/kg DW liver	7
Sodium arsenite	Single oral dose of 5 to 12 mg/kg BW (0.2 to 0.5 g) was acutely toxic	3
Soluble arsenic	Lambs fed supplemental arsenic for 3 months at 2 mg As/kg DW diet contained maximum concentrations of 2 μg/kg FW brain (vs. 1 in controls), 14 in muscle (2), 24 in liver (4), and 57 in kidney (10)	18
Total arsenic	Sheep were fed on diets containing lakeweed, *Lagarosiphon* ***major (288*** mg As/kg DW), at 58 mg total As/kg diet, for 3 weeks without ill effect. Tissue residues increased during feeding, but rapidly declined when lakeweed was removed from diet	7

Table *6 (Continued)*

Organism and Arsenical	Effect	Reference"
Rat, *Rattus* sp.		
Arsanilic acid	No teratogenesis observed in 7 generations at dietary level of 17.5 mg/kg; positive effect on litter size and survival	6
Arsenate	Fed diets containing 50 mg/kg for 10 weeks with no effect on serum uric acid levels	19
Arsenic trioxide	Single oral LD,, (96 hr) value of 15.1 mg/kg BW	12
Arsenic trioxide	Single dose of 17 mg/kg BW administered intratracheally was maximally tolerated nonlethal dose; 2 weeks later, blood As was elevated (36 mg/L) and lung histopathology evident	20
Arsenic trioxide	After 21 days on diet containing 50 mg/kg, tissue arsenic levels were elevated in blood (125 mg/L vs. 15 in controls), heart (43 mg/kg FW vs. 3.3), spleen (60 vs. < 0.7) and kidney (25 vs. 1.5)	7
Arsenite	Oral administration of 1.2 mg/kg BW daily for 6 weeks reduced uric acid levels in plasma by 67%	19
Cacodylic acid	Fetal and maternal deaths noted when pregnant rats were dosed by gavage at 50 to 60 mg/kg BW daily during gestation days 6 to 13. Fetal abnormalities observed when dams given oral dosages of 40 to 60 mg/kg BW on days 7 to 16 of gestation	5
3-Nitro-4-hydroxy-phenylarsonic acid	Single oral LD,, value of 44 mg/kg BW	12
Sodium arsenate	LD,, (48 hr) value of 14 to 18 mg/kg BW (intraperitoneal route)	12
Sodium arsenate	Single intraperitoneal injection of 5 to 12 mg/kg on days 7 to 12 of gestation produced eye defects, exencephaly, and faulty development of kidney and gonads	6
Sodium arsenite	LD,, (48 hr) value of 4.5 mg/kg BW (intraperitoneal injection)	12
Rodents, various species		
Cacodylic acid	LD,, (various routes) values range from 470 to 830 mg/kg BW	5
Sodium cacodylate	LD,, (various routes) values range from 600 to 2600 mg/kg BW	5
Domestic pig, Sus sp.		
Sodium arsenite	Drinking water containing 500 mg/L was lethal at 100 to 200 mg/kg BW	12

Table *6 (Continued)*

Organism and Arsenical	Effect	Reference[a]
3-Nitro-4-hydroxy-phenylarsonic acid	Arsenosis documented after 2 months on diets containing 100 mg/kg, or after 3 to 10 days on diets containing 250 mg/kg	12
Rabbit, *Sylvilagus* sp.		
Cacodylic acid	Adverse effects at dermal dosages equivalent to 4 to 6 g/kg BW	5
Calcium arsenate	Single oral dose of 23 mg/kg BW fatal in 3 days	12
Copper acetoarsenite	Single oral dose of 10.5 mg/kg BW fatal in 50 hr	12
Inorganic arsenate	Single oral LD_{50} value of 8 mg/kg BW	3
Lead arsenate	Single oral dose of 40.4 mg/kg BW fatal in 52 hr	12

[a] I, Vreman et al. (1986); 2, Thatcher et al. (1985); 3, NRCC (1978); 4, Robertson et al. (1984); 5, Hood (1985); 6, Pershagen and Vahter (1979); 7, Woolson (1975); 8, Pershagen and Bjorklund (1985); 9, Belton et al. (1985); 10, Yamauchi et al. (1986); 11, Charbonneau et al. (1978); 12, NAS (1977); 13, Nagymajtenyi et al. (1985); 14, Hood et al. (1987); 15, Stine et al. (1984); 16, Deknudt et al. (1986); 17, Hudson et al. (1984); 18, Veen and Vreman (1985); 19, Jauge and Del-Razo (1985); 20, Webb et a]. (1986).

more toxic than organic arsenic compounds, and trivalent species are more so than pentavalent; (3) inorganic arsenicals can cross the placenta in most mammals; (4) early developmental stages are the most sensitive, and human beings appear to be one of the most susceptible species; (5) animal tissues usually contain low levels ($<$ 0.3 mg As/kg fresh weight) of arsenic; after the administration of arsenicals these levels are elevated, especially in the liver, kidney, spleen, and lung; several weeks later, arsenic is translocated to ectodermal tissues (hair, nails) because of the high concentration of sulfur-containing proteins in these tissues; (6) inorganic arsenicals are oxidized in vivo, biomethylated, and usually excreted rapidly in the urine, but organoarsenicals are usually not subject to similar transformations; (7) acute or subacute arsenic exposure can lead to elevated tissue residues, appetite loss, reduced growth, hearing loss, dermatitis, blindness, degenerative changes in the liver and kidneys, cancer, chromosomal damage, birth defects, and death; (8) death or malformations have been documented at single oral doses of 2.5 to 33 mg As/kg body weight, at chronic doses of 1 to 10 mg As/kg body weight, and at dietary levels $>$ 5 and $<$ 50 mg As/kg diet.

Episodes of wildlife poisoning by arsenic are infrequent. White-tailed deer *(Odocoileus virginianus)* consumed, by licking, fatal amounts of sodium arsenite used to debark trees. The practice of debarking trees with arsenicals for commercial use has been almost completely replaced by mechanical debarking (NAS, 1977). Snowshoe hares (*Lepus* sp.) appear to be especially sensitive to methylated arsenic&; hares died after consuming plants heavily contaminated with mono-

sodium methanearsonate as a result of careless silviculture practices (Hood, 1985).

Unlike wildlife, reports of arsenosis in domestic animals are common in bovines and felines, less common in ovines and equines, and rare in porcines and poultry (NAS, 1977). In practice, the most dangerous arsenic preparations are dips, herbicides, and defoliants in which the arsenical is in a highly soluble trivalent form, usually as trioxide or arsenite (Selby et al., 1977). Accidental poisoning of cattle with arsenicals, for example, is well documented. In one instance, more than 100 cattle died after accidental overdosing with arsenic trioxide applied topically to control lice. On necropsy, there were subcutaneous edematous swellings and petechial hemorrhages in the area of application, and histopathology of the intestine, mucosa, kidneys, and epidermis (Robertson et al., 1984). In Bangladesh, poisoned cattle showed depression, trembling, bloody diarrhea, restlessness, unsteady gait, stumbling, convulsions, groaning, shallow labored breathing, teeth grinding, and salivation (Samad and Chowdhury, 1984b). Cattle usually died 12 to 36 hr after the onset of signs; necropsy showed extensive submucosal hemorrhages of the gastrointestinal tract(Samad and Chowdhury, 1984a), and tissue residues > lOmg/kg fresh weight in the liver and kidneys (Thatcher et al., 1985). It sometimes appears that animals, especially cattle, develop a preference for weeds sprayed with an arsenic weed killer, probably because arsenic compounds are salty and thus attractive to animals (Selby et al., 1977).

When extrapolating animal data from one species to another, the species tested must be considered. For example, the metabolism of arsenic in the rat (*Rattus* sp.) is unique, and very different from that in human beings and other animals. Rats store arsenic in blood hemoglobin, excreting it very slowly--unlike most mammals, which rapidly excrete ingested inorganic arsenic in the urine as methylated derivatives (NAS, 1977). Blood arsenic, whether given as As^{+3} or As^{+5}, rapidly clears from humans, mice, rabbits, dogs, and primates; half-life is 6 hr for the fast phase and about 60 hr for the slow phase (EPA, 1980). In rats, however, blood arsenic is mostly retained in erythrocytes, and clears slowly; half-life is 60 to 90 days (EPA, 1980). In rats, the excretion of arsenic into bile is 40 times faster than in rabbits and up to 800 times faster than in dogs (Pershagen and Vahter, 1979). Most researchers now agree that the rat is unsatisfactory for use in arsenic research (NAS, 1977; NRCC, 1978; Pershagen and Vahter, 1979; EPA, 1980; Webb et al., 1986).

Dimethylarsinic acid is the major metabolite of orally administered arsenic trioxide and is excreted rapidly in the urine (Yamauchi and Yamamura, 1985). The methylation process is true detoxification, since methanearsonates and cacodylates are about 200 times less toxic than sodium arsenite (NAS, 1977). The marmoset monkey (*Callithrix jacchus*), unlike all other animal species studied to date, was not able (for unknown reasons) to metabolize administered As^{+5} to demethylarsinic acid; most was reduced to As^{+3}. Only 20% of the total dose was excreted in urine as unchanged As^{+5}, and another 20% as As^{+3}. The rest was bound to tissues, giving distribution patterns similar to those of arsenite (Vahter

and Marafante, 1985). Accordingly, the marmoset, like the rat, may be unsuitable for research with arsenicals.

Arsenicals were ineffective in controlling certain bacterial and viral infections. Mice experimentally infected with bacteria (*Klebsiella pneumoniae*) or viruses (pseudorabies, encephalitis, encephalmyocarditis) showed a significant increase in mortality when treated with large doses of arsenicals compared with nonarsenic-treated groups (NAS, 1977; Aranyi et al., 1985).

It has been suggested, but not yet verified, that many small mammals avoid arsenic-treated feeds and consume other foods if given the choice (NAS, 1977), and that cacodylic acid, which has negligible effects on wildlife, reduces species diversity due to selective destruction of vegetation (Hood, 1985). Both topics merit more research.

7. RECOMMENDATIONS

Numerous criteria for arsenic have been proposed to protect natural resources and human health (Table 7): But many authorities recognize that these criteria are not sufficient for adequate or (in some cases) reasonable protection, and that many additional data are required if meaningful standards are to be promulgated (NAS, 1977; NRCC, 1978; Pershagen and Vahter, 1979; EPA, 1980, 1985). Specifically, data are needed on the following subjects: (1) cancer incidence and other abnormalities in the natural resources of areas with elevated arsenic levels, and their relation to the potential carcinogenicity of arsenic compounds; (2) interaction effects of arsenic with other carcinogens, cocarcinogens, promoting agents, inhibitors, and common environmental contaminants; (3) controlled studies with aquatic and terrestrial indicator organisms on the physiological and biochemical effects of long-term, low-dose exposures to inorganic and organic arsenicals, including effects on reproduction and genetic makeup; (4) methodologies for establishing maximum permissible tissue concentrations of arsenic; (5) effects of arsenic in combination with infectious agents; (6) mechanisms of arsenical growth-promoting agents; (7) role of arsenic in nutrition; (8) extent of animal adaptation to arsenicals and the mechanisms of action; and (9) physicochemical processes influencing arsenic cycling. In addition, the following techniques and procedures should be developed and implemented: (1) more sophisticated measurements of the chemical forms of arsenic in plant and animal tissues, (2) correlation of biologically observable effects with particular chemical forms of arsenic, and (3) management of arsenical wastes that accommodates recycling, reuse, and long-term storage.

Some proposed arsenic criteria merit additional comment, such as those on aquatic life protection, levels in seafoods and drinking water, and use in food-producing animals as growth stimulants or for disease prevention and treatment.

For saltwater-life protection, the current water-quality criterion of 36 μg As^{+3}/L (EPA, 1985; Table 7) seems to offer a reasonable degree of safety; only a few species of algae show adverse effects at < 36 $\mu g/L$ (e.g., reduced growth at 19

Table 7 Proposed Arsenic criteria for Protection of Selected Natural Resources and Human Health

Resource, Criterion, and Other Variables	Criterion or Effective Arsenic Concentration (reference)
AQUATIC LIFE	
Freshwater biota: medium concentrations	Four-day mean water concentration not to exceed 190 μg total recoverable inorganic As^{+3}/L more than once every 3 years; one-hour mean not to exceed 360 μg inorganic As^{+3}/L more than once every 3 years Insufficient data for criteria formulation for inorganic As^{+5}, or for any organoarsenical (EPA, 1985)
Freshwater biota: tissue residues	Diminished growth and survival reported in immature bluegills when total arsenic residues in muscle > 1.3 mg/kg fresh weight (FW) or > 5 mg/kg in adults (NRCC, 1978)
Saltwater biota: medium concentrations	Four-day average water concentration not to exceed 36 μg As^{+3}/L more than once every 3 years; one-hour mean not to exceed 69 μg As^{+3}/L more than once every 3 years; insufficient data for criteria formulation for inorganic As^{+5}, or for any organoarsenical (EPA, 1985)
Saltwater biota: tissue residues	Depending on chemical form of arsenic, certain marine teleosts may be unaffected at muscle total arsenic residues of 40 mg/kg FW (NRCC, 1978)
BIRDS	
Tissue residues	Residues, in mg total As/kg FW, in liver or kidney in the 2– 10 range are considered elevated; residues > 10 are indicative of arsenic poisoning (Goede, 1985)
Mallard, ***Anus platyrhynchos***	
Sodium arsenate in diet	Reduced growth in ducklings fed > 30 mg As/kg diet (Camardese et al., 1990)
Turkey, *Meleagris gallopavo*	
Arsanilic acid in diet	Maximum dietary concentration for turkeys < 28 days old is 300 to 400 mg/kg feed (NAS, 1977)
Phenylarsonic feed additives for disease control and improvement of weight gain in domestic poultry; safe dietary levels	Maximum levels in diets, in mg/kg feed, are 50 to 100 for arsanilic acid, 25 to 188 for 3-nitro-4-hydroxyphenylarsonic acid (for chickens and turkeys, not

Table *7 (Continued)*

Resource, Criterion, and Other Variables	Criterion or Effective Arsenic Concentration (reference)
	recommended for ducks and geese), and 180 to 370 for others (NAS, 1977)
DOMESTIC LIVESTOCK	
Prescribed limits for arsenic in feedstuffs	
Straight feedstuffs, except those listed below	< 2 mg total As/kg FW (Vreman et al., 1986)
Meals from grass, dried lucerne, or dried clover	< 4 mg total As/kg FW (Vreman et al., 1986)
Phosphate mealstuffs	< 10 mg total As/kg FW (Vreman et al., 1986)
Fish meals	< 10 mg total As/kg FW (Vreman et al., 1986)
Tissue residues	
Poisoned	
Liver, kidney	5 to > 10 mg total As/kg FW (Thatcher et al., 1985; Vreman et al., 1986)
Normal, muscle	< 0.3 mg total As/kg FW (Veen and Vreman, 1985)
VEGETATION	
No observable effects	< 1 mg total water soluble soil As/L; < 25 mg total As/kg soil; < 3.9 $\mu g\ As/m^3$ air (NRCC, 1978)
HUMAN HEALTH	
Diet	
Permissible levels	
Total diet	< 0.5 As/kg dry weight diet (Sorensen et al., 1985)
Fruits, vegetables	Tolerance for arsenic residues as As_2O_3, resulting from pesticidal use of copper, magnesium, and sodium arsenates, is 3.5 mg/kg (Jelinek and Corneliussen, 1977)
Muscle of poultry and swine, eggs, swine edible byproducts	< 0.5 mg total As/kg FW (Jelinek and Corneliussen, 1977)
Edible byproducts of chickens and turkey, liver and kidney of swine	< 2 mg total As/kg FW (Jelinek and Corneliussen, 1977)
Seafood products	In Hong Kong, limited to 6 mg total As/kg FW for edible tissues of finfish, and 10 mg/kg for mollusks and crustaceans (Phillips et al., 1982); in Yugoslavia, these values are 2 for fish and 4 for mollusks and crustaceans (Ozretic et al., 1990)

Table *7 (Continued)*

Resource, Criterion, and Other Variables	Criterion or Effective Arsenic Concentration (reference)
Adverse effects	
Consumption of aquatic organisms living in As-contaminated waters	
Cancer risk of	
10^{-5}	0.175 μg As/L (EPA, 1980)
10^{-6}	0.0175 μg As/L (EPA, 1980)
10^{-7}	0.00175 μg As/L (EPA, 1980)
Drinking water	
Allowable concentrations	
Total arsenic	< 10 μg/L (NAS, 1977)
Total arsenic	50 μg/L (Pershagen and Vahter, 1979; EPA, 1980; Norin et al., 1985)
Adverse effects	
Cancer risk of	
10^{-5}	0.022 μg As/L (EPA, 1980)
10^{-6}	0.0022 μg As/L (EPA, 1980)
10^{-7}	0.00022 μg As/L (EPA, 1980)
Symptoms of arsenic toxicity observed	9% incidence at 50 μg As/L, 16% at 50–100 μg As/L, and 44% at > 100 μg As/L (NRCC, 1978)
Harmful after prolonged consumption	> 50 to 960 μg As/L (NRCC, 1978)
Cancer	In Chile, cancer rate estimated at 0.01% at 82 μg As/L, 0.17% at 600 μg As/L (NRCC, 1978)
Skin Cancer	0.26% frequency at 290 μg/L and 2.14% at 600 μg/L (EPA, 1980)
Total intake	
No observable effect	
North America	0.007 to 0.06 mg As daily (Pershagen and Vahter, 1979)
Japan	0.07 to 0.17 mg As daily (Pershagen and Vahter, 1979)
USA	
1960s	0.05 to 0.1 mg As daily (Pershagen and Vahter, 1979)
1974	0.015 mg As daily (Pershagen and Vahter, 1979)
Canada	0.03 mg As daily (NRCC, 1978)
Netherlands	
Acceptable	2 μg total inorganic As/kg body weight (BW), or about 0.14 mg daily for 70-kg adult; 0.094 mg daily through fishery products (Vos and Hovens, 1986)

Table 7 (Continued)

Resource, Criterion, and Other Variables	Criterion or Effective Arsenic Concentration (reference)
Adverse effects (prolonged exposure)	
Subclinical symptoms	0.15 to 0.6 mg As daily (NRCC, 1978)
Intoxication	3 to 4 mg As daily (NRCC, 1978)
Blackfoot disease	Total dose of 20 g over several years increases prevalence of disease by 3% (Pershagen and Vahter, 1979)
Mild chronic poisoning	0.15 mg As daily or about 2 μg/kg BW daily (NRCC, 1978)
Chronic arsenicism	Lifetime cumulative absorption of 1 g As, or intake of 0.7 to 2.6 g/year for several years (in medications) can produce symptoms after latent period of 4 to 24 years (NRCC, 1978)
Tissue residues	
No observed effect levels	
Urine	< 0.05 mg As/L (NRCC, 1978)
Liver, kidney	< 0.5 mg As/kg FW (NRCC, 1978)
Blood	< 0.7 mg As/L (NRCC, 1978)
Hair	< 2 mg As/kg FW (NRCC, 1978)
Fingernail	< 5 mg As/kg FW (NRCC, 1978)
Arsenic-poisoned	
Liver, kidney	2 to 100 mg As/kg FW; confirmatory tests > 10 mg As/kg FW; residues in survivors several days later were 2 to 4 mg/kg FW (NAS, 1977)
Whole body	In child, symptoms of chronic arsenicism evident at 1 mg As/kg BW, equivalent to intake of about 10 mg/month for 3 months; for adults, values were 80 mg/kg BW, equivalent to about 2 g/year for 3 years (NRCC, 1978)
Air	
Allowable concentrations	
Arsine	< 200 μg/m^3 for USA industrial workers; proposed mean arsine limit of < 4 μg/m^3 in 8-hr period and < 10 μg/m^3 maximum in 15 minutes (NAS, 1977)
Arsine	< 4 μg/m^3 (NRCC, 1978)
Total As	< 3 μg/m^3 in former USSR and Czechoslovakia; < 500 μg/m^3 for USA industrial workers (NAS, 1977)
Total As (threshold limit value-time weighted average: 8 hr/day, 40 hr week)	Proposed limit of < 50 μg/m^3, maximum of 2 μg/m^3 in 15 minutes, < 10 μg airborne inorganic As/m^3 (EPA, 1980)

Table *7 (Continued)*

Resource, Criterion, and Other Variables	Criterion or Effective Arsenic Concentration (reference)
Arsenic trioxide	$< 0.3\ \mu g/m^3$ in former USSR, $< 0.1\ \mu g/m^3$ in USA (Nagymajtenyi et al., 1985)
Adverse effects	
Increased mortality	Associated with daily time-weighted average As exposure of $> 3\ \mu g/m^3$ for one year (NRCC, 1978)
Respiratory cancer (increased risk)	Associated with chronic exposure $> 3\ \mu g$ As/m^3, or occupational exposure (lifetime) of $> 54.6\ \mu g\ As/m^3$ (NRCC, 1978)
Respiratory cancer (increased risk)	Exposure to $50\ \mu g\ As/m^3$ for more than 25 years associated with 3X increase (Pershagen and Vahter, 1979)
Skin diseases	Associated with ambient air concentrations of 60 to $13{,}000\ \mu g\ As/m^3$ (NRCC, 1978)
Dermatitis	Associated with ambient air concentrations of 300 to $81{,}500\ \mu g\ As/m^3$ (NRCC, 1978)

[a] One excess cancer per million population (10^{-6}) is estimated during lifetime exposure to 0.0022 μg arsenic per liter of drinking water, or to lifetime consumption of aquatic organisms residing in waters containing 0.0175 μg As/L (EPA, 1980)

to 22 $\mu g/L$). In 1980, this criterion was 508 $\mu g/L$ (EPA, 1980), about 14 times higher than the current criterion. The downward modification seems to be indicative of the increasingly stringent arsenic criteria formulated by regulatory agencies. The current criterion for freshwater-life protection of 190 $\mu g\ As^{+3}/L$ (EPA, 1985; Table 7), however, which is down from 440 $\mu g\ As^{+3}/L$ in 1980 (EPA, 1980), is unsatisfactory. Many species of freshwater biota are adversely affected at $< 190\ \mu g/L$ of As^{+3}, As^{+5}, and various organoarsenicals (Table 4). These adverse effects include death and malformations of toad embryos at 40 $\mu g/L$, growth inhibition of algae at 48 to 75 $\mu g/L$, mortality of amphipods and gastropods at 85 to 88 $\mu g/L$, and behavioral impairment of goldfish (*Carassius auratus*) at 100 $\mu g/L$. A downward adjustment in the current freshwater aquatic-life protection criterion seems warranted.

In Hong Kong, permissible concentrations of arsenic in seafood destined for human consumption range from 6 to 10 mg/kg fresh weight (Table 7); however, these values are routinely exceeded in 22% of finfish, 20% of bivalve mollusks, 67% of gastropods, 29% of crabs, 21% of shrimp and prawns, and 100% of lobsters (Phillips et al., 1982). The highest arsenic concentrations recorded in Hong Kong seafood products were in gastropods (*Hemifusus* spp.), in which the concentrations of 152 to 176 mg/kg fresh weight were among the highest recorded in any species to date (Phillips et al., 1982). A similar situation exists in

Yugoslavia, where almost all seafoods exceed the upper limit prescribed by food quality regulations (Ozretic et al., 1990). Most of the arsenic in seafood products is usually arsenobetaine or some other comparatively harmless form. In effect, arsenic criteria for seafoods are neither enforced nor enforceable. Some toxicologists from the U.S. Food and Drug Administration believe that the average daily intake of arsenic in different foods does not pose a hazard to the consumer (Jelinek and Corneliussen, 1977).

For maximum protection of human health from the potential carcinogenic effects of exposure to arsenic through drinking water or contaminated aquatic organisms, the ambient water concentration should be zero, based on the nonthreshold assumption for arsenic. But zero level may not be attainable. Accordingly, the levels established are those that are estimated to increase cancer risk over a lifetime to only one additional case per 100,000 population. These values are estimated at 0.022 μg As/L for drinking water and 0.175 μg As/L for water containing edible aquatic resources (EPA, 1980; Table 7).

Various phenylarsonic acids-especially arsanilic acid, sodium arsanilate, and 3-nitro-4-hydroxyphenylarsonic acid-have been used as feed additives for disease control and for improvement of weight gain in swine and poultry for almost 40years (NAS, 1977). The arsenic is present as As^{+5} and is rapidly excreted; present regulations require withdrawal of arsenical feed additives 5 days before slaughter for satisfactory depuration (NAS, 1977). Under these conditions, total arsenic residues in edible tissues do not exceed the maximum permissible limit of 2 mg/kg fresh weight (Jelinek and Corneliussen, 1977). Organoarsenicals probably will continue to be used as feed additives unless new evidence indicates otherwise.

8. CONCLUDING REMARKS

Arsenic is a teratogen and carcinogen that can traverse placental barriers and produce fetal death and malformations in many species of mammals. Although it is carcinogenic in humans, evidence for arsenic-induced carcinogenicity in other mammals is scarce. Paradoxically, evidence is accumulating that arsenic is nutritionally essential or beneficial. Arsenic deficiency effects, such as poor growth, reduced survival, and inhibited reproduction, have been recorded in mammals fed diets containing $<$ 0.05 mg As/kg, but not in those fed diets with 0.35 mg As/kg. At comparatively low doses, arsenic stimulates growth and development in various species of plants and animals.

Most arsenic produced domestically is used in the manufacture of agricultural products such as insecticides, herbicides, fungicides, algicides, wood preservatives, and growth stimulants for plants and animals. Living resources are exposed to arsenic via atmospheric emissions from smelters, coal-fired power plants, and arsenical herbicide sprays; via water contaminated by mine tailings, smelter wastes, and natural mineralization; and via diet, especially consumption of marine biota. Arsenic concentrations are usually low ($<$ 1.0 mg/kg fresh

weight) in most living organisms, but they are elevated in marine biota (in which arsenic occurs as arsenobetaine and poses little risk to organisms or their consumer) and in plants and animals from areas that are naturally arseniferous or that are near industrial manufacturers and agricultural users of arsenicals. Arsenic is bioconcentrated by organisms but is not biomagnified in the food chain.

Arsenic exists in four oxidation states, as inorganic or organic forms. Its bioavailability and toxic properties are significantly modified by numerous biological and abiotic factors, including the physical and chemical forms of arsenic tested, the route of administration, the dose, and the species of animal. In general, inorganic arsenic compounds are more toxic than organic compounds, and trivalent species are more toxic than pentavalent species. Arsenic may be absorbed by ingestion, inhalation, or through permeation of the skin or mucous membranes; cells take up arsenic through an active transport system normally used in phosphate transport. The mechanisms of arsenic toxicity differ greatly among chemical species, although all appear to cause similar signs of poisoning. Biomethylation is the preferred detoxification mechanism for absorbed inorganic arsenicals; methylated arsenicals usually clear from tissues within a few days.

Episodes of arsenic poisoning are either acute or subacute; chronic cases of arsenosis are seldom encountered in any species except human beings. Single oral doses of arsenicals fatal to 50% of the sensitive species tested ranged from 17 to 48 mg/kg body weight in birds and from 2.5 to 33 mg/kg body weight in mammals. Susceptible species of mammals were adversely affected at chronic doses of 1 to 10 mg As/kg body weight, or 50mg As/kg diet; mallard ducklings were negatively affected at dietary concentrations as low as 30 mg/kg ration. Sensitive aquatic species were damaged at water concentrations of 19 to 48 μg As/L (the U.S. Environmental Protection Agency drinking-water criterion for human health protection is 50 μg/L), 120 mg As/kg diet, or (in the case of freshwater fish) tissue residues $>$ 1.3 mg/kg fresh weight. Adverse effects on crops and vegetation were recorded at 3 to 28 mg of water-soluble As/L (equivalent to about 25 to 85 mg total As/kg soil) and at atmospheric concentrations $>$ 3.9 μg As/m^3.

Numerous and disparate arsenic criteria have been proposed for the protection of sensitive natural resources; however, the consensus is that many of these criteria are inadequate and that additional information is needed in at least five categories: (1) developing standardized procedures to permit correlation of biologically observable effects with particular chemical forms of arsenic; (2) conducting studies under controlled conditions with appropriate aquatic and terrestrial indicator organisms to determine the effects of chronic exposure to low doses of inorganic and organic arsenicals on reproduction, genetic makeup, adaptation, disease resistance, growth, and other variables; (3) measuring interaction effects of arsenic with other common environmental contaminants, including carcinogens, cocarcinogens, and promoting agents; (4) monitoring the incidence of cancer and other abnormalities in the natural resources of areas with relatively high arsenic levels, and correlating these with the possible carcinogenicity of arsenic compounds; and (5) developing appropriate models of arsenic cycling and budgets in natural ecosystems.

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