# 9. EFFECTS ON OTHER ORGANISMS IN THE ENVIRONMENT

## 9.1 Laboratory experiments

The toxic effects of arsenicals are significantly modified by numerous biological and abiotic factors. The toxicity of arsenic in the environment is affected by temperature, pH, Eh, organic content, phosphate concentration, adsorption to solid matrices, the presence of other substances and toxicants, duration of exposure and the arsenic species present. In general, inorganic arsenicals are more toxic than organoarsenicals to biota, and trivalent species are more toxic than pentavalent species for both inorganic and organic arsenic compounds (NAS, 1977; NRCC, 1978; Eisler, 1988).

### *9.1.1 Microorganisms*

#### *9.1.1.1 Water*

Aquatic microorganisms show a wide range of sensitivities to arsenic species, with arsenite generally being more toxic than arsenate. Resistance to arsenic species has been reported in micro-organisms. The toxicity of arsenate is decreased by increasing the phosphate concentration, whereas the inhibitory effect of arsenite is independent of phosphate.

Bringmann & Kühn (1977, 1978) exposed the bacterium *P. putida* for 16 h and the cyanobacteria *Microcystis aeroginosa* for 8 days to arsenate. The toxic thresholds for the inhibition of cell multiplication were found to be 8.1 and 7.3 mg As(V)/litre respectively.

Growth under phosphate-limiting conditions (20 µmol/litre) of the blue-green alga *Synechococcus leopoliensis* was unaffected by arsenate < 15 mg As(V)/litre (200 µmol/litre) (Budd & Craig, 1981). Arsenite concentrations > 3.75 mg As(III)/litre (50 µmol/litre) inhibited the growth of *S. leopoliensis* but the inhibition was transitory with growth resuming after a lag period the length of which was related to the arsenite exposure. The growth of algae

which had been previously exposed to arsenite (0.75 mg As(III)/litre (10 µmol/litre) for 12 h) was unaffected at 15 mg As(III)/litre (200 µmol/litre) (Budd et al., 1986).

Arsenate at ≥30 mg As(V)/litre completely inhibited growth of a marine cyanobacterium (*Phormidium* sp.) when incubated in the absence of phosphate (Takahashi et al., 1990). However, at a phosphate concentration of 50 µmol/litre no effect on growth was observed at 150 mg As(V)/litre. Thiel (1988) reports that arsenate was a poor non-competitive inhibitor of phosphate transport in the cyanobacterium *Anabaena variabilis* with a $K_i$ of 82.5 mg As(V)/litre (1.1 mmol/litre). In cells starved of phosphate for 3 days, arsenate was almost completely non-competitive with a $K_i$ of 5.6 mg As(V)/litre (75 µmol/litre). Preincubation of phosphate-starved cells with arsenate caused subsequent inhibition of phosphate transport, suggesting that intracellular arsenate inhibited phosphate transport.

Toxicity of arsenic to microalgae is summarized in Table 37. $EC_{50}$s, based on growth, range from 48 µg As(V)/litre to 202 mg As(V)/litre (14 days). Blum (1966) found that arsenate competitively inhibits phosphate uptake by green algae *Euglena gracilis*. The authors report that arsenate has almost as high an affinity for the transport system as does phosphate, although arsenate is accumulated at a much lower rate than phosphate.

Hörnström (1990) examined the toxicity of arsenate to a variety of algal species in 72–96-h tests. The most tolerant group was the Chrysophyceae, with four of the five species tested having a no-observed-effect concentration (NOEC) of 500 µg As(V)/litre. Chlorophyceae including *Chlamydomonas* sp. and *Scenedesmus denticulatus*, *Bacillariophyceae* and *Cryptophyceae* show a lowest observed effect concentration (LOEC) of 50 µg/litre. The most sensitive alga was a Chrysophyte *Stichogloea doederleinii* with a LOEC of 5 µg As(V)/litre.

Bringmann & Kuhn (1977) exposed the green alga *Scenedesmus quadricauda* to arsenate for 8 days. They found the toxic threshold for the inhibition of cell multiplication to be 3.5 mg As(V)/litre. Maeda et al. (1985) found that the growth of microalgae (*Chlorella vulgaris*) isolated from an arsenic-polluted environment was unaffected at arsenate concentrations of 2000 mg As(V)/litre.

Table 37. Toxicity of As to microalgae[a]

| Organism | Stat/ flow | Tempera-ture (°C) | pH | Salt | Duration | EC50 (mg As/litre) | Reference |
|---|---|---|---|---|---|---|---|
| **Freshwater** | | | | | | | |
| Green algae | | | | | | | |
| *Scenedesmus quadricauda* | stat | 25 | 8.0 | arsenate | 12 d | 61 n (59.3–70.1) | Fargasova (1994a) |
| *Scenedesmus obliquus* | stat | 24 | 7.0 | arsenate | 14 d | 0.048 | Vocke et al. (1980) |
| *Ankistrodesmus falcatus* | stat | 24 | 7.0 | arsenate | 14 d | 0.26 | Vocke et al. (1980) |
| *Selenastrum capricornutum* | stat | | | arsenite | 96 h | 31.2 | US EPA (1985) |
| | stat | | | arsenate | 96 h | 0.69 | US EPA (1985) |
| | stat | 24 | 7.0 | arsenate | 14 d | 30.8 | Vocke et al. (1980) |
| *Chlamydomonas reinhardii* | stat | 20 | 7.0 | arsenate | 14 d | 202 | Jurewicz & Buikema (1980) |
| **Marine** | | | | | | | |
| Diatom | | | | | | | |
| *Nitzschia closterium* | stat | 21 | 8.1 | arsenate | 72 h | >2 | Florence et al. (1994) |
| | stat | 21 | 8.1 | arsenite | 72 h | 0.007 | Florence et al. (1994) |

[a] stat = static conditions (water unchanged for duration of test; $EC_{50}$s based on growth); n = based on nominal concentrations

Michnowicz & Weaks (1984) studied the effects of pH on the toxicity of arsenate to *Selenastrum capricornutum* in 14-day tests. Growth was significantly enhanced at pH 6, 8, 10 and 12 compared with pH 4, with optimum growth at pH 10. Addition of arsenate (0.2 mg/litre) inhibited growth over the range of pH values tested; growth of cultures at pH 8 was significantly higher than at pH 4. No significant difference in arsenate-induced growth inhibition was observed at 7 and 14 days, indicating that no arsenic toxicity occurred after 7 days.

In 14-day growth inhibition tests with *Chlamydomonas reinhardii* stimulation of the biomass occurred at arsenate concentrations of < 151 mg As(V)/litre with maximum stimulation (73% above controls) at 100 mg As(V)/litre (Jurewicz & Buikema, 1980).

Conway (1978) found no significant effect on growth or micronutrient utilization of the freshwater diatom *Asterionella formosa* exposed to 160 µg As(V)/litre (as arsenate) for < 23 days.

Growth and survival of the marine microalgae *Tetraselmis chui* and *Hymenomonas carterae* were not affected during a 6-day exposure to concentrations as high as 1 mg As/litre of arsenite or arsenate (Bottino et al., 1978).

Growth of *Dunaliella* sp. was inhibited during exposure for 3 days to arsenate concentrations of ≥100 µg As(V)/litre, but during continued exposure growth rate recovers and is normal after 12 days at concentrations < 2 mg As(V)/litre (Yamaoka & Takimura, 1986).

Hollibaugh et al. (1980) studied the toxicity of arsenic to *Thalassiosira aestevalis* in 4-day tests. Arsenate had no effect on growth at 75 µg As(V)/litre (1000 nmol/litre) in a high-phosphate medium. Growth was reported to be repressed by both arsenate and arsenite at > 22.5 µg As/litre (300 nmol/litre) in a low-phosphate medium; however, no statistical analysis was carried out on these results.

Sanders (1979b) exposed the diatom *Skeletonema costatum* to arsenate, arsenite and DMA for 6–8 days. Growth was significantly inhibited at arsenate and arsenite concentrations of 12.5 µg As/litre

(167 nmol/litre). DMA had no effect on growth at 9.8 µg As/litre (130 nmol/litre). Arsenate and arsenite additions of ≥5 µg As/litre (67 nmol/litre) caused significant inhibition of $^{14}C$ uptake by *Skeletonema* during both log and stationary phases; however, DMA had no significant effect on carbon uptake at 25.5 µg As/litre (340 nmol/litre). Additions of phosphate (20 µmol/litre) to the media eliminated the arsenate inhibition of carbon uptake.

Knauer et al. (1999) investigated the toxicity of arsenic species to natural phytoplankton assemblages from contaminated lakes within the Aberjona watershed (USA) using short-term photosynthesis bioassays. The toxicity of the arsenic species generally decreased in the order arsenate > arsenite > DMA. Toxicity of arsenate to phytoplankton collected from an unpolluted lake was highest ($EC_{50}$ = $3 \times 10^{-7}$ mol/litre), whereas algae from polluted lakes were more tolerant ($EC_{50}$ = $3 \times 10^{-6}$ mol/litre). The sensitivities of the different algal communities to arsenite were similar ($EC_{50}$ = $5 \times 10^{-5}$ mol/litre). Long-term studies with cultures of natural phytoplankton communities exposed to low levels of arsenate (1B15 µg As(V)/litre) showed that pentavalent arsenic differentially inhibits certain plants, causing a change in species composition, succession and predator–prey relationships (Sanders & Vermersch, 1982; Sanders & Cibik, 1985, 1988; Sanders, 1986). Arsenate inputs caused declines in large centric diatoms and replacement by a smaller diatom (*Th. pseudonana*) and small flagellates. Sanders & Riedel (1987) suggest two mechanisms by which algal species may be less sensitive to arsenate and, therefore, dominate exposed communities. Resistant species may have a higher affinity for phosphate and thus a lower uptake rate of arsenate, or some species may be able to transform it intracellularly into a less toxic form (Sanders & Riedel, 1987).

Blanck & Wängberg (1988b) established 1 h $IC_{20}$s for arsenate, based on inhibition of photosynthesis, for both natural marine periphyton communities and laboratory-established communities under low-phosphate conditions. Although there were substantial differences between the communities in terms of structure and biomass, $IC_{20}$s were similar at 30 µg As(V)/litre (0.4 µmol/litre) and 45 µg As(V)/litre (0.6 µmol/litre) respectively. In longer-term studies (3 weeks) similar values for $IC_{20}$s (15–60 µg As(V)/litre; 0.2–0.8 µmol/litre) were established for changes in species

composition, and reductions in carbon, nitrogen and chlorophyll *a* content. Blanck & Wängberg (1988a) found that marine periphyton communities previously exposed to arsenate concentrations from 7.5 to 22.5 µg As(V)/litre (0.1 –0.3 µmol/litre) showed increased resistance to arsenate. The authors concluded that arsenate exerts a selection pressure on the community, leading to the replacement of sensitive species with tolerant ones which causes the overall arsenate tolerance of the community to increase. Pre-exposure to arsenate at 750 µg As(V)/litre (10 µmol/litre) increased arsenate tolerance of the community by a factor of 16 000 (Blanck & Wängberg, 1991).

Wängberg & Blanck (1990) found that increasing the phosphate concentration from 0.1 to 0.8 µmol/litre decreased the toxicity of arsenate to marine periphyton communities in 72 h tests by > 3000-fold $EC_{20}$ values based on carbon dioxide fixation increased from 22.5 µg: As(V)/litre to > 75 mg/litre (0.3 µmol/litre to > 1 mmol/litre). Similar changes in toxicity were observed during natural upwelling episodes during which both phosphate and nitrate concentrations increased.

#### *9.1.1.2 Soil*

Soil microorganisms show wide variation in resistance to arsenic species.

The toxicity of arsenate (As(V)), as measured by retardation or inhibition of growth in 8-week tests, showed wide variation among different species of fungi. Toxicity was consistently reduced by the addition of phosphate with both arsenate-sensitive and arsenate-tolerant strains. *Poria monticola*, an arsenate-sensitive fungus, was completely inhibited by 187.5 mg As(V)/kg (0.0025 mol/litre) but was progressively less inhibited as the phosphate concentration increased and some growth occurred at 3000 mg As(V)/kg (0.04 mol/litre) when 0.16 mol/litre potassium phosphate was added. An arsenate-tolerant fungus, *Cladosporium herbarum*, showed 36% reduction in growth at 6000 mg As(V)/kg (0.08 mol/litre) but when 0.01 mol/litre phosphate was added there was no effect on growth at arsenate concentrations of 48 g As(V)/kg (0.64 mol/litre). Addition of phosphate also reduced the toxicity of arsenite (As(III)) but not DMA (Da Costa, 1972). The counteracting effect of phosphate on arsenate toxicity was found to occur with all of the fungi tested and with the bacteria *Bacillus subtilis* and *P. aeruginosa*.

Sharples et al. (1999) found $EC_{50}$s for arsenate, based on growth inhibition, for the endomycorrhizal fungus *Hymenoscyphus ericae* and the ectomycorrhizal fungus *Hebeloma crustuliniforme* to be 99.6 mg As(V)/litre (1.33 mol/$m^3$) and 24.7 mg As(V)/litre (0.33 mol/$m^3$) respectively. The presence of phosphate (0.01B1.0 mol/$m^3$) in the media ameliorated the toxic effects of arsenate.

#### 9.1.1.3 Bacterial resistance to arsenic

Burton (1987) collected heterotrophic bacteria from a variety of contaminated sites and found that < 0.21% were resistant to arsenite at 750 mg As(III)/litre (10 mmol/litre). Resistance to arsenite was much lower than that reported for selenite (54%) at the same sites.

Huysmans & Frankenberger (1990) isolated arsenic-resistant bacteria from contaminated agricultural drainage water. Plasmid-mediated arsenic-resistant bacteria have now been widely found in various sources. Several of the systems have been cloned and sequenced; closely related arsenic resistance systems are found on plasmids and the chromosome of *Escherichia coli* and plasmids of *Staphylococcus* (Rosenstein et al., 1992; Ji & Silver, 1995). The mechanisms of bacterial resistance are reviewed and discussed in detail by Ji & Silver (1995). Genes on bacterial plasmids have been identified that encode specific resistance systems for arsenic. The chromosomally encoded arsenical resistance (*ars*) operon was found in all strains of *E. coli* but not in *Salmonella typhimurium*, *P. aeruginosa* or *B. subtilis* (Carlin et al., 1995). Bröer et al. (1993) demonstrated energy-dependent accelerated arsenite efflux from *Staphylococcus aureus* cells with the cloned resistance determinant. In Gram-negative bacteria, the efflux pump consists of a complex formed by an ATPase (ArsA) associated with a membrane anion channel (ArsB). Arsenate is converted to arsenite by a soluble reductase (ArsC). Proteins ArsA and ArsB, but not the ATPase, are also found in Gram-positive bacteria (Cervantes, 1995). Other than plasmid arsenic resistance determinants, some bacteria also have the ability to oxidize arsenite to arsenate enzymatically (see section 4.2.1).

Suzuki et al. (1997) isolated the acidophilic bacterium *Acidiphilium multivorum* from acid mine drainage in Japan. Bacteria

were found to be resistant to arsenite at concentrations < 1125 mg As(III)/litre (15 mmol/litre). Baldi et al. (1995) isolated arsenic-resistant bacteria (750 mg/litre sodium arsenite) from mosses growing near geothermal plants (south-west of Siena, Italy).

Growth of *P. putida* was not impaired by arsenate concentrations of 1000 mg As(V)/litre (Maeda et al., 1990b). Huysmans & Frankenberger (1990) isolated bacteria from agricultural drain water and exposed the organisms to arsenic compounds for 48 h. Arsenate, MMA and DMA had no effect on colony-forming units at concentrations < 1000 mg/litre. However, arsenite concentrations > 1 mg/litre inhibited the population. Similar results were found with sediment, with no effect at an arsenate concentration of 1000 mg As/kg and increases in colony-forming units at MMA or DMA concentrations > 25 mg/kg, but arsenite concentrations > 100 mg/kg caused a decline in colony-forming units. In further tests, the arsenic-resistant bacteria showed a high tolerance to a variety of metals and antibiotics.

### *9.1.2 Aquatic organisms*

#### *9.1.2.1 Macroalgae*

Growth was significantly reduced at 212 µg As(III)/litre, and at 300 µg/litre all plants died. Phosphate concentrations of < 9.1 µmol/litre had no effect on arsenite toxicity. Concentrations of 10 mg/litre arsenate did not cause mortality, but sexual reproduction did not occur at this concentration. The toxicity of arsenate increased as the phosphate concentration decreased (Thursby & Steele, 1984).

#### *9.1.2.2 Aquatic plants*

Jenner & Janssen-Mommen (1993) studied the effect of arsenite and arsenate on the growth of the duckweed *Lemna minor*. They reported 14-day $EC_{50}$ values, based on growth inhibition, of 0.63 mg As(III)/litre and 22.2 mg As(V)/litre, and NOECs of < 0.75 mg As(III)/litre and < 4 mg As(V)/litre. Sarkar & Jana (1986) found the floating aquatic heterosporous fern *Azolla pinnata* to be resistant to arsenic in 28-day tests. No significant effect on growth, photosynthesis, chlorophyll and protein content or tissue permeability were observed at arsenate concentrations of 1 mg As(V)/litre.

#### 9.1.2.3 Invertebrates

Acute toxicity of inorganic arsenic to freshwater and marine invertebrates is summarized in Tables 38 and 39 respectively. In general, arsenite appears to be more toxic than arsenate in acute tests. The 48-h $LC/EC_{50}$ values range from 0.68 to 73.5 mg/litre for trivalent arsenic and from 3.6 to 49.6 mg/litre for pentavalent arsenic. However, the lowest acute value is for the nauplius stage of the marine copepod *Tigriopus brevicornis*, with a 96-h $LC_{50}$ of 10.9 µg As(V)/litre. Acute toxicity of organic arsenicals to aquatic invertebrates is summarized in Table 40. The 48-h $LC_{50}$ values for MMA range from 17.4 mg As/litre to 2361 mg As/litre.

Schaefer & Pipes (1973) found that the acute toxicity of arsenate to rotifers (*Philodina roseola*) increased with increasing temperature (5 to 35 °C). For example, the 96-h $LC_{50}$ was 18 mg As(V)/litre at 5 °C and 6.6 mg As(V)/litre at 35 °C. Bryant et al. (1985) exposed three estuarine invertebrates (*Corophium volutator*, *Macoma balthica* and *Tubifex costatus*) to pentavalent arsenic for < 384 h. Median survival times decreased as temperature (5, 10 and 15 °C) and concentration of arsenic (1 to 128 mg As(V)/litre) increased but salinity changes (5 to 35 g/litre) had no significant effect. The presence of sediment consistently reduced the acute toxicity (48 h) of trivalent arsenic to *D. magna* in repeated tests. The toxicity had been reduced by a factor of 5 within 6 days and by a factor of 16 within 49 days (Burton et al., 1987). Golding et al. (1997) found that the freshwater snail *Potamopyrgus antipodarum* was insensitive to arsenic in avoidance tests. The 48-h $EC_{50}$s for arsenite and arsenate, based on immobilization, were 34.6 mg As(III)/litre and 325 mg As(V)/litre for snails from a contaminated site (0.3 mg As/litre), and 19.3 mg As(III)/litre and 194 mg As(V)/litre for a control site. The authors report that previously exposed snails appear to be more sensitive to the presence of arsenate and arsenite; in avoidance experiments snails from a contaminated site showed significant avoidance at 15 mg As(III)/litre whereas control snails responded at 28 mg As(III)/litre.

Spehar et al. (1980) found no significant effect on survival or young production of *D. magna* exposed to either arsenite, arsenate, MMA (disodium salt) or DMA (sodium salt) at 1 mg/litre in 14-day tests. In a 7-day test on *Ceriodaphnia dubia* the maxiumum

allowable toxicant concentration (MATC) for arsenite was found to be 1.1 mg As(III)/litre, with production of young being the most sensitive parameter (Spehar & Fiandt, 1986). In 15-day tests there was no effect on the survival of the estuarine copepod *Eurytemora affinis* at arsenate concentrations of 50 µg/litre; however, concentrations of ≥100 µg/litre caused a significant increase in the mortality of juveniles. Adult copepod survival was significantly reduced at arsenate concentrations of 1 mg/litre (Sanders, 1986).

On the basis of survival and reproductive impairment of *D. magna*, 21-day $EC_{50}$s were found to be 2.9 and 1.4 mg As(V)/litre (as arsenate) respectively at a water hardness of 45 mg $CaCO_3$/litre (Biesinger & Christensen, 1972). However, Naddy et al. (1995) found no significant effect of arsenate on fecundity of *C. dubia* at 1.42 mg As(V)/litre when tested at 120 mg $CaCO_3$/litre. Enserink et al. (1991) report a 21-day $LC_{50}$ for arsenic pentoxide of 5.8 mg As(V)/litre (semi-static test) for D. magna with an $EC_{50}$ of 3.2 mg As(V)/litre on the basis of population effects (survival, body growth, rate of population increase and maximum yield) under flow-through conditions. Lima et al. (1984) found that daphnid survival, production of young and mean total length of adults were significantly reduced at ≥1320 µg As(III)/litre (as arsenite) in 28-day tests. The NOEC was between 633 and 1320 µg/litre for these parameters.

Ettajani et al. (1996) found no effect of arsenic-spiked sediments (20.5 mg As(V)/kg) or dissolved (10 µg As(V)/litre) arsenate on survival of oysters (*Crassostrea gigas*). Structural alterations of mitochondria and nuclei in arsenic-exposed oysters were observed by electron microscopy.

Naqvi & Flagge (1990) exposed crayfish to MMA at a concentration of 46 mg As/litre for 168 days. There was no significant effect on the number of eggs laid, but arsenic significantly reduced the number of eggs that hatched. No significant effect was observed on growth or moulting frequency of newly hatched crayfish exposed to 6.9 mg As/litre (as MMA).

Cowell (1965) found that arsenite concentrations of 4 mg As(III)/litre caused significant reductions in populations of zooplankton (rotifers, copepods and cladocerans) in experimental

Table 38. Toxicity of inorganic As to freshwater invertebrates

| Organism | Size/ age | Stat/ flow | Temper- ature ($^{o}$C) | Hardness (mg/litre) | pH | As species | Duration (h) | $LC_{50}$ (mg As/litre) | Reference |
|---|---|---|---|---|---|---|---|---|---|
| Snail *Aplexa hypnorum* | adult | stat | 25 | 49.5 | 7.4–7.7 | $As_2O_3$ | 96 | 18.6 m | Holcombe et al. (1983) |
| Tubificid worm *Tubifex tubifex* | 20 mm | stat | 20 | NS | 7.4 | arsenate | 96 | 127.4 (108.8–134.3) n | Fargasova (1994a) |
| Amphipod *Gammarus pseudolimnaeus* | NS | flow | 18.5 | 46.3–49.9 | 7.2–8.1 | arsenite | 96 | 0.87 m | Lima et al. (1984) |
| Water fleas | NS | stat | 18 | 45 | 7.7 | arsenate | 48 | 7.4 n | Biesinger & Christensen (1972) |

Table 38 (contd).

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| *Daphnia magna* | NS | stat | 15.6 | 46.3–49.9 | 7.2–8.1 | arsenite | 48 | 1.5 (1.2–1.9) ! m | Lima et |
| | NS | stat | 15.6 | 46.3–49.9 | 7.2–8.1 | arsenite | 48 | 4.6 (3.7–5.8) !! m | al. (1984) |
| | 6–24 h | stat | 20 | NS | 7.3 | arsenate | 48 | 44.7 (35.2–50.9) n | Fargasova (1994a) |
| | NS | stat | NS | NS | NS | arsenite | 48 | 2.1 & 6.6 | Burton et al. (1987) |
| | 1st instar | stat | 15 | 44 | 7.4 | arsenite | 48 | 1.7 (1.3–2.4) @ | Mayer & Ellersieck (1986) |
| *Daphnia pulex* | NS | stat | NS | NS | NS | arsenate | 48 | 3.6 (3.3–3.9) m | Jurewicz & Buikema (1980) |
| | >24 h | stat | 17 | 120 | 6.8 | arsenate | 48 | 49.6 (48.7–50.5) @ n | Passino & Novak (1984) |
| *Ceriodaphnia dubia* | <24 h | stat | 25 | 100 | 8.2 | arsenite | 48 | 1.5 (1.2–1.7) | Spehar & Fiandt (1986) |

Table 38 (contd.)

| Organism | Size/ age | Stat/ flow | Temper-ature ($^{o}$C) | Hardness (mg/litre) | pH | As species | Duration (h) | $LC_{50}$ (mg As/litre) | Reference |
|---|---|---|---|---|---|---|---|---|---|
| *Simocephalus serrulatus* | 1st instar | stat | 16 | 44 | 7.4 | arsenite | 48 | 0.8 (0.6–1.1) @ | Mayer & Ellersieck (1986) |
| Cladoceran | | | | | | | | | |
| *Bosmina longirostris* | <24 h | stat | 17 | 120 | 6.8 | arsenate | 96 | 0.85 (0.7–1.0) @ n | Passino & Novak (1984) |
| Midges | | | | | | | | | |
| *Chironomus tentans* | 3$^{rd}$ instar | stat | 14 | 25 | 6.3 | | 48 | 0.68 @ n | Khangarot & Ray (1989) |
| *Tanytarsus dissimilis* | 3$^{rd}$/4$^{th}$ instar | stat | 24 | 47 | 7.2–7.7 | $As_2O_3$ | 48 | 73.5 (72–75) m | Holcombe et al. (1983) |
| Stonefly | | | | | | | | | |
| *Pteronarcys californica* | 1$^{st}$ year class | stat | 15 | 44 | 7.4 | arsenite | 96 | 21.9 (17.3–27.7) | Mayer & Ellersieck (1986) |

stat = static conditions (water unchanged for duration of test); hardness expressed as mg $CaCO_3$/litre; @ = $EC_{50}$s based on immobilization; ! = unfed; !! = fed; n = based on nominal concentrations; m = based on measured concentrations

Table 39. Toxicity of inorganic As to marine invertebrates

| Organism | Size/ age | Stat/ flow | Temper- ature ($^{o}$C) | Salinity (g/litre) | pH | As species | Duration (h) | $LC_{50}$ (mg As/litre) | Reference |
|---|---|---|---|---|---|---|---|---|---|
| Eastern oyster | | | | | | | | | |
| *Crassostrea virginica* | juvenile | flow | 15 | 22 | NS | $As_2O_3$ | 96 | > 0.75 # n | Mayer (1987) |
| | juvenile | flow | 13 | 31 | NS | arsenate | 96 | > 0.4 # n | Mayer (1987) |
| Pacific oyster | | | | | | | | | |
| *Crassostrea gigas* | embryo | stat | 20 | 34 | 8.1 | $As_2O_3$ | 48 | 0.33 ## n | Martin et al. (1981) |
| Mussel | | | | | | | | | |
| *Mytilus edulis* | embryo | stat | 17 | 34 | 8.1 | $As_2O_3$ | 48 | > 3.0 ## n | Martin et al. (1981) |
| Bay scallop | | | | | | | | | |
| *Argopecten irradians* | juvenile | stat$ | 20 | 25 | NS | arsenite | 48 | 4.4 n | Nelson et al. (1976) |
| | juvenile | stat$ | 20 | 25 | NS | arsenite | 96 | 3.5 (2.1–5.8) n | |
| Polychaete worm | | | | | | | | | |
| *Neanthes arenaceodentata* | NS | flow | NS | NS | NS | arsenite | NS | 10.1 m | US EPA (1985) |

Table 39 (contd.)

| Organism | Size/ age | Stat/ flow | Temper- ature (°C) | Salinity (g/litre) | pH | As species | Duration (h) | $LC_{50}$ (mg As/litre) | Reference |
|---|---|---|---|---|---|---|---|---|---|
| Dungeness crab | | | | | | | | | |
| *Cancer magister* | zoeae | stat | 15 | 34 | 8.1 | $As_2O_3$ | 96 | 0.23 n | Martin et al. (1981) |
| Intertidal crab | | | | | | | | | |
| *Scylla serrata* | 60–70 mm* | stat$ | 26.5–29.5 | NS | 7.0–7.2 | $As_2O_3$ | 48 | 23 (18–29.4) n | Krishnaja et al. (1987) |
| | 60–70 mm* | stat$ | 26.5–29.5 | NS | 7.0–7.2 | $As_2O_3$ | 96 | 17 (13.4–21.4) n | |
| Amphipods | | | | | | | | | |
| *Elasmopus bampo* | 8–12 mm | stat | 19 | NS | NS | $As_2O_3$ | 96 | 2.8 (1.8–4.3) n | Reish (1993) |
| *Corophium insidiosum* | 8–12 mm | stat | 19 | NS | NS | $As_2O_3$ | 96 | 1.1 (0.8–1.6) n | Reish (1993) |
| Copepods | NS | stat | NS | NS | NS | arsenite | 96 | 0.51 n | US EPA (1985) |
| *Acartia clausi* | nauplius | stat$ | 20 | 35 | 7.7–8.1 | arsenate | 96 | 0.011 (0.009–0.013) n | Forget et al. (1998) |
| *Tigriopus brevicornis* | copepodid | stat$ | 20 | 35 | 7.7–8.1 | arsenate | 96 | 0.02 (0.018–0.022) n | |
| | ovigerous female | stat$ | 20 | 35 | 7.7–8.1 | arsenate | 96 | 0.028 (0.025–0.03) n | Forget et al. (1998) |

Table 39 (contd.)

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Harpacticoid copepod | | | | | | | | | |
| *Nitocra spinipes* | adult | stat | 20–22 | 3 | NS | arsenite | 96 | 3.5 (2.8–4.3) n | Bengtsson & |
| | adult | stat | 20–22 | 7 | NS | arsenate | 96 | 3.0 (2.1–4.2) n | Bergstr m (1987) |
| Mysid shrimp | NS | flow | NS | NS | NS | arsenite | 96 | 1.7 m | US EPA (1985) |
| *Mysidopsis bahia* | NS | flow | NS | NS | NS | arsenate | 96 | 2.3 m | US EPA (1985) |
| Pink shrimp | | | | | | | | | |
| *Penaeus duorarum* | juvenile | stat | 19 | 24 | NS | $As_2O_3$ | 48 | >30 @ n | Mayer (1987) |
| | juvenile | stat | 19 | 24 | NS | arsenate | 48 | >15 @ n | Mayer (1987) |
| White shrimp | | | | | | | | | |
| *Penaeus setiferus* | juvenile | stat | 22 | 25 | 8.3–8.7 | As trisulfide | 96 | 24.8 (19.1–35.2) n | Curtis et al. (1979) |

stat = static conditions (water unchanged for duration of test); stat$ = static renewal conditions (water replaced on a regular basis); flow = flow-through conditions (As concentration continuously maintained);NS = not stated; * = carapace breadth; # = $EC_{50}$s based on inhibition of shell deposition; ## = $EC_{50}$s based on abnormal development; @ = $EC_{50}$s based on immobilization; n = based on nominal concentrations; m = based on measured concentrations

**Table 40.** Toxicity of organic As to aquatic invertebrates

| Organism | Size/ age | Stat/ flow | Temper- ature (°C) | Hardness (mg/litre) | pH | Arsenical | Duration (h) | $LC_{50}$ (mg As/litre) | Reference |
|---|---|---|---|---|---|---|---|---|---|
| Scud | | | | | | | | | |
| *Gammarus fasciatus* | mature | stat | 15 | 44 | 7.4 | MMA (34.8%) | 96 | >16 | Mayer & Ellersieck (1986 |
| Cladoceran | | | | | | | | | |
| *Alonella* sp. | NS | stat | 20 | 15 | 7.8 | MMA | 48 | 18.2 | Naqvi et al. (1985) |
| Calanoid | | | | | | | | | |
| *Diaptomus* sp. | NS | stat | 20 | 15 | 7.8 | MMA | 48 | 17.4 | Naqvi et al. (1985) |
| Cyclopoid | | | | | | | | | |
| *Eucyclops* sp. | NS | stat | 20 | 15 | 7.8 | MMA | 48 | 44.6 | Naqvi et al. (1985) |
| Ostracod | | | | | | | | | |
| *Cypria* sp. | NS | stat | 20 | 15 | 7.8 | MMA | 48 | 45.5 | Naqvi et al. (1985) |
| Crayfish | NS | stat | NS | NS | NS | MMA | 48 | 2361 n | Anderson et al. (1975) |
| *Procambarus* sp. | NS | stat | NS | NS | NS | MMA | 96 | 509 n | Anderson et al. (1975) |
| *Procambarus clarkii* | juvenile | stat | 21–27 | NS | 5.8–7.8 | MMA | 96 | 46.7 | Naqvi et al. (1987) |
| | adult | stat | 21–27 | NS | 5.8–7.8 | MMA | 96 | 472 | Naqvi et al. (1987) |

stat = static conditions (water unchanged for duration of test); NS = not stated; hardness expressed as mg $CaCO_3$/litre; MMA = monomethylarsonic acid (administered as the monosodium salt); $EC_{50}$s based on growth; n = based on nominal concentrations

ponds. Sanders (1986) studied the effect of arsenate (15 µg/litre) on zooplankton survival in natural phytoplankton assemblages over 24 days. After 10 days the arsenate-treated tanks contained phytoplankton assemblages dominated by the centric diatom *Th. pseudonana*, whereas control tanks contained a variety of algal species, although flagellates became increasingly more important. By the end of the experiment zooplankton density in control tanks was 2–3 times higher than in arsenate-treated tanks. No significant effect on survival of a natural assemblage of copepods was observed when organisms were exposed to arsenate at < 10 mg As(V)/litre for 2 weeks; however, arsenite caused significant mortality at both 4 and 10 mg As(III)/litre (Borgmann et al., 1980).

#### *9.1.2.4 Vertebrates*

Acute toxicity of arsenic to freshwater and marine fish is summarized in Tables 41 and 42 respectively. The 96-h $LC_{50}$s for freshwater fish range from 10.8 to 91 mg/litre for trivalent arsenic and from 4.8 to > 360 mg/litre for pentavalent arsenic. In marine fish 96-h $LC_{50}$s range from 12.7 to 28.5 mg As(III)/litre and from 21.4 to 157 mg As(V)/litre. Acute toxicity of organic arsenicals to fish is summarized in Table 43. $LC_{50}$s for the organic arsenical MMA range from 1.9 to 1412 mg As/litre.

McGeachy & Dixon (1989) found no effect of temperature on arsenite toxicity to rainbow trout (*O. mykiss*) with 144-day $LC_{50}$s of 17.7 and 20.7 mg/litre at 5 and 15 °C respectively. However, arsenate toxicity was increased from an $LC_{50}$ of 114.1 mg/litre at 5 °C to 58 mg/litre at 15 °C.

Most of the data on the effects of arsenic on fish are based on acute toxicity tests which measure fish mortality over 96 h. Some studies have also examined sub-lethal effects such as growth, avoidance behaviour and fertilization/hatching.

Nichols et al. (1984) exposed coho salmon (*O. kisutch*) fry to $As_2O_3$ (30, 100 or 300 µg As(III)/litre) for 6 months in freshwater; smolting fry were transferred to seawater (salinity 28 g/litre) for a further 6 months. Survival and growth were unaffected by arsenic exposure. Migration of trout released after the arsenic exposure was significantly reduced at the highest concentration.

Table 41. Toxicity of inorganic As to freshwater fish

| Organism | Size/ age | Stat/ flow | Temper- ature (°C) | Hardness (mg/litre) | pH | As species | Duration (h) | $LC_{50}$ (mg As/litre) | Reference |
|---|---|---|---|---|---|---|---|---|---|
| Chinook salmon | | | | | | | | | |
| *Oncorhynchus* | 0.5 g | stat | 12 | 211 | 7.0–8.3 | $As_2O_3$ | 96 | 25.1 (19.3–32.7) n | Hamilton & |
| *tshawytscha* | 0.5 g | stat | 12 | 211 | 3.4–7.2 | As pentoxide | 96 | 90 (70–116) n | Buhl |
| | 1 g | stat | 12 | 211 | 6.9–7.4 | As pentoxide | 96 | 167 (120–233) * n | (1990) |
| Coho salmon | | | | | | | | | |
| *Oncorhynchus kisutch* | alevin | stat | 12 | 41 | 7.1–8.0 | arsenite | 96 | 49.4 (42.1–57.9) n | Buhl & |
| | juvenile | stat | 12 | 41 | 7.1–8.0 | arsenite | 96 | 18.5 (14.5–23.7) n | Hamilton (1991) |
| | alevin | stat | 12 | 41 | 7.1–8.0 | arsenate | 96 | 306 (216–433) n | Buhl & |
| | 0.41 g | stat | 12 | 41 | 7.1–8.0 | arsenate | 96 | 43.6 (32.5–58.5) n | Hamilton |
| | 0.47 g | stat | 12 | 41 | 7.1–8.0 | As pentoxide | 96 | 58.5 (49.4–69.3) n | (1990) |
| Rainbow trout | | | | | | | | | |
| *Oncorhynchus mykiss* | 2.6 g | stat | 12 | 44 | 7.4 | arsenite | 96 | 13.3 (7.8–22.5) | Mayer & Ellersieck (1986) |
| | alevin | stat | 12 | 41 | 7.1–8.0 | arsenite | 96 | 91 (69.9–119) n | Buhl & |
| | juvenile | stat | 12 | 41 | 7.1–8.0 | arsenite | 96 | 16 (12.7–20.1) n | Hamilton (1991) |
| | alevin | stat | 12 | 41 | 7.1–8.0 | arsenate | 96 | >360 n | Buhl & |
| | 0.6 g | stat | 12 | 41 | 7.1–8.0 | arsenate | 96 | 67.5 (56.1–81.2) n | Hamilton (1990) |

Table 41 (contd.)

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Brook trout<br>*Salvelinus fontinalis* | adult | flow | 15 | 152 | 7.8 | arsenite | 96 | 15 m | Cardwell et al. (1976) |
| Bluegill<br>*Lepomis macrochirus* | 0.8 g | stat | 24 | 50 | 7.3–8.0 | arsenite | 96 | 15.2 n | Inglis & Davis (1972) |
| | 0.8 g | stat | 24 | 210 | 7.5–8.0 | arsenite | 96 | 16.2 n | |
| | 0.8 g | stat | 24 | 370 | 7.7–8.0 | arsenite | 96 | 15.4 n | |
| | 1 g | stat | 24 | 44 | 7.4 | arsenite | 96 | 17.3 (12.3–24.4) | Mayer & Ellersieck (1986) |
| | juvenile | flow | 25 | 147 | 7.8 | arsenite | 96 | 41.6 m | Cardwell et al. (1976) |
| Fathead minnow<br>*Pimephales promelas* | juvenile | stat | 22 | 25 | 8.3–8.7 | As trisulfide | 96 | 82.4 (65.4–105.9) n | Curtis et al. (1979) |
| | juvenile | flow | 25 | 149 | 7.8 | arsenite | 96 | 15.6 m | Cardwell et al. (1976) |
| | NS | flow | 23–25.8 | 46.3–49.9 | | arsenite | 96 | 14.1 (12.5–15.9) m | Lima et al. (1984) |
| | 0.15 g | flow | 22–28 | 43.9 | 6.0–8.1 | arsenite | 96 | 12.6 (9.9–15.9) | Spehar & Fiandt (1986) |
| | | | | | | arsenate | 96 | 25.6 | US EPA (1985) |

Table 41 (contd.)

| Organism | Size/ age | Stat/ flow | Temper- ature (°C) | Hardness (mg/litre) | pH | As species | Duration (h) | $LC_{50}$ (mg As/litre) | Reference |
|---|---|---|---|---|---|---|---|---|---|
| Goldfish | | | | | | | | | |
| *Carassius auratus* | 4–8 cm | stat | 23 | NS | 6.0–6.9 | arsenate | 48 | 32 (24.6–41.6) n | Weir & Hine (1970) |
| | juvenile | flow | 25 | 148 | 7.6 | arsenite | 96 | 26 m | Cardwell et al. (1976) |
| | | | | | | arsenate | 96 | 34 | US EPA (1985) |
| Golden shiner | | | | | | | | | |
| *Notemigonus crysoleucas* | NS | flow | NS | 72.2 | 7.5 | arsenite | 96 | 12.5 (10.0–14.6) m | Hartwell et al. (1989) |
| Striped bass | | | | | | | | | |
| *Morone saxatilis* | 63 d | stat | 20 | 40 | 8.1 | As pentoxide | 96 | 40.5 (32–51.2) n | Palawski et |
| | 63 d | stat | 20 | 285 | 7.9 | As pentoxide | 96 | 30.5 (21.3–43.7) n | al. (1985) |
| Colorado squawfish | | | | | | | | | |
| *Ptychocheilus lucius* | larvae | stat | 25 | 144 | 8.1 | arsenate | 96 | 105 (74–164) n | Hamilton & Buhl (1997) |
| Razorback sucker | | | | | | | | | |
| *Xyrauchen texanus* | larvae | stat | 25 | 144 | 8.1 | arsenate | 96 | 17.8 (13.7–21.3) n | Hamilton & Buhl (1997) |

Table 41 (contd.)

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Flagfish | | | | | | | | | |
| *Jordanella floridae* | fry | flow | 25 | NS | NS | arsenite | 96 | 28 m | Cardwell et al. (1976) |
| | juvenile | flow | 23–25.8 | 46.3–49.9 | NS | arsenite | 96 | 14.4 (12.7–16.3) m | Lima et al. (1984) |
| Arctic grayling | | | | | | | | | |
| *Thymallus arcticus* | alevin | stat | 12 | 41 | 7.1–8.0 | arsenite | 96 | 27.7 (23.5–32.7) n | Buhl & |
| | juvenile | stat | 12 | 41 | 7.1–8.0 | arsenite | 96 | 13.7 (11.6–16.1) n | Hamilton (1991) |
| | fry | stat | 12 | 41.3 | 7.1–8.0 | As pentoxide | 96 | 5.0 (3.5–7.2) n | Buhl & |
| | 0.2 g | stat | 12 | 41.3 | 7.1–8.0 | As pentoxide | 96 | 4.8 (3.8–5.9) n | Hamilton (1990) |
| | 0.34 g | stat | 12 | 41.3 | 7.1–8.0 | As pentoxide | 96 | 5.5 (4.1–7.5) n | Buhl & |
| | alevin | stat | 12 | 41.3 | 7.1–8.0 | arsenate | 96 | 102 (75–141) n | Hamilton (1990) |
| | alevin | stat | 12 | 41.3 | 7.1–8.0 | arsenate | 96 | 197 (145–267) n | Buhl & |
| | 0.85 g | stat | 12 | 41.3 | 7.1–8.0 | arsenate | 96 | 47.7 (35–65) n | Hamilton (1990) |
| | 0.97 g | stat | 12 | 41.3 | 7.1–8.0 | arsenate | 96 | 32.5 (25.3–41.6) n | Buhl & |
| | 1.85 g | stat | 12 | 41.3 | 7.1–8.0 | arsenate | 96 | 30.9 (21.9–43.6) n | Hamilton (1990) |

Table 41 (contd.)

| Organism | Size/ age | Stat/ flow | Temper- ature ($^{o}$C) | Hardness (mg/litre) | pH | As species | Duration (h) | $LC_{50}$ (mg As/litre) | Reference |
|---|---|---|---|---|---|---|---|---|---|
| Channel catfish *Ictalurus punctatus* | juvenile | flow | 25 | 140 | 8.0 | arsenite | 96 | 18 m | Cardwell et al. (1976) |
| Murrel *Channa punctatus* | fingerling | stat | 24 | 124 | 7.2 | $As_2O_3$ | 96 | 10.8 (9.9–12.7) n | Shukla et al. (1987) |
| Mosquito fish *Gambusia affinis* | NS | stat | 20 | NS | NS | arsenate | 96 | 49 (44–54) | Jurewicz & Buikema (1980) |
| Deepwater ciscoe (chub) *Coregonus* sp. | fry | stat | 7 | NS | NS | $As_2O_3$ | 96 | 17 (13–22) n | Passino & Kramer (1980) |

Stat = static conditions (water unchanged for duration of test); flow = flow-through conditions (As concentration continuously maintained); NS = not stated; hardness expressed as mg $CaCO_3$/litre; *, pH buffered; n = based on nominal concentrations; m = based on measured concentrations

Table 42. Toxicity of inorganic As to marine fish

| Organism | Size/ age | Stat/ flow | Temper- ature (°C) | Salinity (g/litre) | pH | As species | Duration (h) | $LC_{50}$ (mg As/litre) | Reference |
|---|---|---|---|---|---|---|---|---|---|
| Chinook salmon | | | | | | | | | |
| *Oncorhynchus* | 1.99 g | stat | 12 | brackish | 6.7–8.4 | $As_2O_3$ | 96 | 21.4 (18.1–25.3) n | Hamilton & |
| *tshawytscha* | 1.99 g | stat | 12 | brackish | 2.7–6.0 | As pentoxide | 96 | 66.5 (55.4–79.8) n | Buhl (1990) |
| | 1.99 g | stat | 12 | brackish | 6.9–7.4 | As pentoxide | 96 | 157 (119–208) * n | Hamilton & Buhl (1990) |
| Sheepshead minnow | | | | | | | | | |
| *Cyprinodon variegatus* | NS | flow | NS | NS | NS | Arsenite | NS | 12.7 m | US EPA (1985) |
| Atlantic silverside | | | | | | | | | |
| *Menidia menidia* | NS | stat | NS | NS | NS | arsenite | NS | 16 n | US EPA (1985) |
| Fourspine stickleback | | | | | | | | | |
| Apeltes quadracus | NS | stat | NS | NS | NS | arsenite | NS | 15 n | US EPA (1985) |
| Longnose killifish | | | | | | | | | |
| *Fundulus similis* | juvenile | stat | 16 | 31 | NS | $As_2O_3$ | 48 | >30 n | Mayer (1987) |
| | juvenile | stat | 16 | 31 | NS | arsenate | 48 | >15 n | Mayer (1987) |

Table 42 (contd.)

| Organism | Size/ age | Stat/ flow | Temper- ature (°C) | Salinity (g/litre) | pH | As species | Duration (h) | $LC_{50}$ (mg As/litre) | Reference |
|---|---|---|---|---|---|---|---|---|---|
| Striped bass | | | | | | | | | |
| *Morone saxatilis* | 1.8 g | stat | 20 | 22 | NS | arsenate | 96 | 10.3 (6.4–13.5) | Dwyer et al. (1992) |
| *Therapon jarbua* | 0.2–0.7 g | stat | NS | 36 | NS | arsenite | 96 | 3.38 | Krishna-kumari et al. (1983) |
| Dab | | | | | | | | | |
| *Limanda limanda* | 16.9 g | flow | 12 | 34.6 | 7.7 | arsenite | 96 | 28.5 (22.7–36.0) m | Taylor et al. (1985) |
| Grey mullet | | | | | | | | | |
| *Chelon labrosus* | 0.87 g | flow | 12 | 34.6 | 7.7 | arsenite | 96 | 27.3 (23.4–30.2) m | Taylor et al. (1985) |

stat = static conditions (water unchanged for duration of test); flow = flow-through conditions (As concentration continuously maintained); NS = not stated; salinity measured in mg/litre; * = pH buffered; n = based on nominal concentrations; m = based on measured concentrations

Table 43. Toxicity of MMA to freshwater fish

| Organism | Size/ age | Stat/ flow | Temper- ature (°C) | Hardness (mg/litre) | pH | Arsenical | Duration (h) | $LC_{50}$ (mg As/litre) | Reference |
|---|---|---|---|---|---|---|---|---|---|
| Rainbow trout | | | | | | | | | |
| *Oncorhynchus mykiss* | 0.6 g | stat | 12 | 44 | 7.4 | MMA (51.2%) | 96 | 18.5 (14.2–23.9) | Mayer & Ellersieck (1986) |
| Bluegill | | | | | | | | | |
| *Lepomis macrochirus* | 0.9 g | stat | 18 | 44 | 7.1 | MMA (34.8%) | 96 | 1.9 n | Mayer & |
| | 1.0 g | stat | 17 | 44 | 7.1 | MMA (37.7%) | 96 | 8.6 (4.4–16.7) | Ellersieck |
| | 1.0 g | stat | 22 | 44 | 7.4 | MMA (51.2%) | 96 | > 23.7 | (1986) |
| Fathead minnow | | | | | | | | | |
| *Pimephales promelas* | 0.9 g | stat | 18 | 44 | 7.1 | MMA (34.8%) | 96 | 2.1 (0.8–5.8) n | Mayer & Ellersieck (1986) |
| Goldfish | | | | | | | | | |
| *Carassius auratus* | 0.9 g | stat | 18 | 44 | 7.1 | MMA (34.8%) | 96 | 5 (3.9–6.3) n | Mayer & Ellersieck (1986) |

Table 43 (contd.)

| Organism | Size/ age | Stat/ flow | Temper- ature (°C) | Hardness (mg/litre) | pH | Arsenical | Duration (h) | $LC_{50}$ (mg As/litre) | Reference |
|---|---|---|---|---|---|---|---|---|---|
| Channel catfish | | | | | | | | | |
| *Ictalurus lacustris* | NS | stat | NS | NS | NS | MMA | 96 | 1412 n | Anderson et al. (1975) |
| | 2.1 g | stat | 17 | 44 | 7.1 | MMA (37.7%) | 96 | 4.7 (3.5–6.3) | Mayer & Ellersieck (1986) |
| Black bass | | | | | | | | | |
| *Micropterus dolmieu* | NS | stat | NS | NS | NS | MMA | 96 | 417 n | Anderson et al. (1975) |

stat = static conditions (water unchanged for duration of test); NS = not stated; hardness expressed as mg $CaCO_3$/litre;
MMA = monomethylarsonic acid; n = based on nominal concentrations

Lima et al. (1984) exposed fathead minnow (*Pimephales promelas*) and flagfish (*Jordanella floridae*) to arsenite in 29-day and 31-day tests respectively. Growth was significantly reduced at concentrations of 4300 and 4120 µg As(III)/litre for the two species respectively. The NOEC, based on growth, was between 2130 and 4300 µg As(III)/litre for *P. promelas* and between 2130 and 4120 µg As(III)/litre for *J. floridae*. Spehar et al. (1980) found no significant effect on survival of rainbow trout exposed to either arsenite (961 µg As(III)/litre), arsenate (973 µg As(V)/litre), MMA (970 µg As/litre) or DMA (846 µg As/litre) in 28-day tests. Growth of fingerling freshwater murrel (*Channa punctatus*) was significantly reduced by $As_2O_3$ at 7 mg As(III)/litre during a 31-day test (Shukla et al., 1987). In 32-day tests on *P. promelas*, growth was found to be the most sensitive parameter, the MATC being 3.3 mg As(III)/litre (Spehar & Fiandt, 1986).

Cockell & Hilton (1985) found no adverse effect on rainbow trout fed diets containing 10–90 mg As(V)/kg arsenate for 16 weeks or 120–1600 mg As/kg DMA or arsanilic acid for 8 weeks. In 28-day tests a significant reduction in growth was observed at all dietary concentrations of 137–1477 mg As(III) or As(V)/kg (as $As_2O_3$ and sodium arsenate). However, no significant adverse effects could be found at concentrations of < 1497 mg As/kg for the organic arsenicals DMA and arsanilic acid (Cockell & Hilton, 1988). Cockell et al. (1991) found the MATC for arsenate to be between 13 and 33 mg As(V)/kg diet (0.281 to 0.525 mg As/kg body weight) in 12-week and 24-week tests. The most sensitive indicator of chronic dietary toxicity was inflammation of the gallbladder wall. Oladimeji et al. (1984) reported that rainbow trout fed on a diet containing arsenite at 20 or 30 mg As(III)/kg (equivalent to 0.2, 0.4 and 0.6 mg/kg fish wet weight per day) for 8 weeks showed significantly reduced growth. No effect on growth was noted at 10 mg As(III)/kg.

Weir & Hine (1970) found a significant impairment of avoidance behaviour at 100 µg As(V)/litre (as arsenate) but no effect at 50 µg/litre on goldfish (*Carassius auratus*). The avoidance threshold for golden shiner (*Notemigonus crysoleucas*) was 28 µg As(III)/litre (as arsenite) in flow-through tests (Hartwell et al., 1989).

Birge et al. (1978) exposed rainbow trout (*O. mykiss*), largemouth bass (*Micropterus salmoides*) and marbled salamander

(*Ambystoma opacum*) to arsenite from fertilization to 4 days after hatching. Treatment periods were 8 days for bass and salamander, and 28 days for trout. $LC_{50}$s were 0.54, 42.1 and 4.45 mg As(III)/litre for trout, bass and salamander respectively. Similar embryo–larval stage tests carried out by Birge (1978) revealed 7-day $LC_{50}$ values of 0.49 and 0.04 mg As(III)/litre for goldfish (*C. auratus*) and narrow-mouthed toad (*Gastrophryne carolinensis*) respectively. Khangarot et al. (1985) found 48-day and 96-h $LC_{50}$s for *Rana hexadactyla* tadpoles to be 0.27 and 0.25 mg As(III)/litre respectively in static tests with $As_2O_3$.

### 9.1.3 Terrestrial organisms

#### 9.1.3.1 Plants

The phytotoxic actions of inorganic and organic arsenicals are modified by the environment in which the plant is growing. Dominant factors include iron, aluminium, calcium and phosphate content of the soil, and pH. Levels of soil arsenic reported to be toxic to plants span a broad range. In general, arsenate is less toxic to plants than arsenite. The primary mechanism of arsenite toxicity is considered to be due to its binding with protein sulfhydryl groups (Peoples, 1975). Arsenite penetrates the plant cuticle to a greater degree than arsenate (NAS, 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 involves chlorosis but not rapid loss of turgor (NAS, 1977). Arsenate is known to uncouple phosphorylation by replacing phosphate; the coupled oxidative phosphorylation of adenosine diphosphate is blocked. Organoarsenicals such as DMA enter plants mostly by absorption of sprays; uptake from the soil contributes only a minor fraction. The phytotoxicity of organoarsenical herbicides is characterized by chlorosis, cessation of growth, gradual browning, dehydration, and death (NAS, 1977). There is a much better correlation between plant growth and available arsenic than between plant growth and total arsenic (Woolson et al., 1971; Woolson, 1973; Walsh & Keeney, 1975).

Davis et al. (1978) grew barley in sand treated with a nutrient solution to which arsenate had been added. The upper critical level (minimum concentration in actively growing tissues of a plant at

which yield is reduced) in the leaves and shoots of barley plants was 20 mg As(V)/kg (dry weight). Fargasová (1994b) grew mustard seeds (*Sinapis alba*) in nutrient solution and calculated a 72-h $LC_{50}$, based on germination, and an $EC_{50}$, based on root growth inhibition, at 30.2 mg As(V)/litre and 5.5 mg As(V)/litre respectively. Neumann et al. (1998) performed tests with alfalfa seedlings inoculated with *Rhizobium meliloti* for 14 days. $EC_{50}$s, based on a reduction in nodulation, were 2.6, 5.5 and 20.1 µmol/litre As for arsenate, arsenite and arsenic pentoxide respectively. Inhibition of nodulation was two orders of magnitude more sensitive than the inhibition of root and shoot growth. Vaughan & Greensdale (1998) found that seedling emergence of *Lactuca sativa* was more sensitive to arsenite ($EC_{50}$ 6.15 mg/kg, 120 h exposure) than arsenate ($EC_{50}$ 26.1 mg/kg). Similarly, root elongation of *L. sativa* was inhibited by lower levels of arsenite ($EC_{50}$ 0.6 mg/litre, 120 h exposure) than arsenate ($EC_{50}$ 2.3 mg/litre).

Carbonell-Barrachina et al. (1998) grew the perennial marsh plants *Spartina patens* and *S. alterniflora* in nutrient solution at arsenate, arsenite, DMA and MMA concentrations of 0.2, 0.8 and 2 mg/litre for 30 days. Plant growth (total dry biomass production) was significantly reduced at all three exposure concentrations when the source of arsenic was DMA. However, arsenate at the lower two concentrations, and arsenite at the lowest concentration, caused a significant increase in growth and this was accompanied by an increase in plant phosphate content. The highest arsenic concentration caused a significant reduction in growth when plants were exposed to either arsenate or arsenite. MMA caused a significant increase in growth of *S. patens* at both 0.2 and 0.8 mg As/litre; however, all exposures of MMA to *S. alterniflora* caused significant decreases in growth.

Sheppard (1992) reviewed phytotoxic levels of arsenic in soil and found that the source of arsenic had the largest effect on mean toxic levels in soils with inorganic and waste forms of arsenic significantly less toxic than organic sources. Waste forms of arsenic include solid mineral forms where much of the arsenic would be occluded. For inorganic sources, arsenic is 5-fold more toxic in sands (toxicity threshold 40 mg/kg) than in clay soils (toxicity threshold 200 mg/kg), on the basis of geometric means.

Woolson (1973) found that growth was reduced by 50% at arsenate levels ranging from 0.7 to 87 mg As(V)/kg (in edible tissues) for six different vegetable varieties. The authors report that available arsenic accounts for 64–83% of the variation in plant growth. Woolson et al. (1971) grew corn seedlings for 4 weeks in Lakeland loamy soil contaminated with arsenic compounds. Growth was reduced by 50% at a sodium arsenate concentration of 42 mg As(V)/kg. Iron, aluminium and calcium arsenate compounds were between 13% and 62% less toxic.

Jiang & Singh (1994) found that application rates of arsenite and arsenate at ≥50 mg As(III) or As(V)/kg caused significant reductions in the yield of ryegrass (*Lolium perenne*) and barley (*Hordeum vulgare*). However, application of an NPK fertilizer containing < 3000 mg As(III)/kg did not affect yield, although increases in arsenic residues were observed. The yield reduction due to arsenic application was greater in sand than in loam soil. The higher arsenic retention capacity of the latter soil was due to its higher content of iron and aluminium oxides.

Anastasia & Kender (1973) grew lowbush blueberry (*Vaccinium angustifolium*) in a loamy sand containing $As_2O_3$. Growth was significantly inhibited at ≤69.5 mg As(III)/kg soil; significant reductions in growth were observed at foliar concentrations of 6.7 mg As/kg.

Deuel & Swoboda (1972b) determined toxicity levels for $As_2O_3$ to cotton (*G. hirsutum*) and soybean (*Glycine max*) in a 6-week greenhouse experiment using fine sandy loam and clay soils. Significant reductions in cotton yield were observed at 56 and 280 kg As(III)/ha for the two soil types respectively. Soybeans were found to be more sensitive, with significant reductions in yield at 28 and 168 kg As(III)/ha respectively. The application rates at which significant yield reductions were observed were related to water-soluble arsenic levels of 8 and 28 mg As(III)/litre for cotton and 3 and 12 mg As(III)/litre for soybeans. The authors found that the critical plant tissue concentrations with regard to yield were ≥4.4 mg As/kg for cotton and ≥1 mg/kg for soybeans. Weaver et al. (1984) found that 90 mg As(III)/kg (as $As_2O_3$) essentially prevented growth of Bermuda grass (*Cynodon dactylon*) on silt loam and fine sand, and significantly reduced growth on clay soil. No significant effect on

growth was observed at 45 mg As(III)/kg for the clay and at 10 mg/kg for the other two soil types.

Jacobs et al. (1970b) found significant reductions in the yield of peas (*Pisum sativum*), snap beans (*Phaseolus vulgaris*) and sweet corn (*Zea mays*) at sodium arsenite application rates ≥80 kg As(III)/ha in field studies on sandy soil. Woolson & Isensee (1981) report significant reductions in the yield of soybean (*G. max*) and radish (*Raphanus sativus*) at 89.6 kg As(III)/ha (10 times the recommended application rate) each year during a 7-year trial. DMA (112 kg/ha) and MMA (56 kg/ha) caused significant reductions in yield during some years but not consistently throughout the experiment.

Schweizer (1967) observed a significant reduction in growth (height) of cotton (*G. hirsutum*) after 4 weeks at ≥80 mg DSMA/kg in a silt loam. Significant adverse effects on the fresh weight and height of rice and soybean, and on the fresh weight alone of corn, cotton and oats, were noted at 50 mg DSMA/kg. Baker et al. (1969) found no effect of MSMA and DSMA on cotton when applied to weeds as a directed spray at 0.4–0.6 kg/ha; however, when applied topically to the cotton plants both arsenic compounds caused significant reductions in yield. Arle & Hamilton (1971) applied MSMA and DSMA topically to cotton plants. Single applications of DSMA at rates of 2.2–9 kg/ha had no significant effect on cotton seed yield; however, MSMA significantly reduced yield at ≥ 6.7 kg/ha. Two or more applications of 2.2 kg MSMA/ha also caused significant reductions in yield. Significant adverse effects were observed on average cotton boll components with multiple applications of DSMA, and to a greater extent MSMA. Keeley & Thullen (1971) found that MSMA (with or without 0.5% surfactant) was significantly more toxic to cotton at 13 °C than at 20 °C or 31 °C when applied to the foliage at a rate of 3.36 kg/ha. Similarly, DSMA was significantly more toxic at 13 °C than at higher temperatures but only with the addition of 0.5% surfactant.

Since arsenic has been found to persist in soil at toxic levels after application of arsenate insecticides, much work has been focused on the alleviation of arsenic toxicity by a variety of means. Laboratory studies have shown that the addition of sufficient phosphate can depress uptake of arsenate by plants. Woolson et al. (1973) found that when sufficient phosphate was added to a sandy

loam soil (P/As ratio 7) improved yields were observed. However, at very high arsenic concentrations (1000 mg/kg) phosphate did not overcome arsenate toxicity. Woolson et al. (1973) pointed out that in soils in which added phosphate desorbs arsenate, leaching of the soil after addition of phosphate may be a viable approach to removing arsenic from the root zone. Steevans et al. (1972) attempted to alleviate arsenic toxicity on a sandy soil by application of 4 t/ha of ferric sulfate or aluminium sulfate. The iron treatment had a slight beneficial effect but the aluminium treatment actually depressed yields further.

Tolerance of plants to arsenic has been identified. Macnair & Cumbes (1987) found that the growth of the grass *Holcus lanatus* (non-tolerant strain) was significantly reduced at a nutrient solution arsenate concentration of 5 mg As(V)/litre (0.067 mmol/litre) in a 7-day test. However, no effect on growth was observed in a tolerant strain at 10 mg As(V)/litre (0.133 mmol/litre). The addition of phosphate (0.1 mmol/litre) at the lowest arsenate concentration (5 mg/litre, 0.067 mmol/litre) reduced arsenic toxicity in non-tolerant strains significantly more than for tolerant plants. Similarly, Meharg & Macnair (1991b) found that the addition of phosphate at 0.5 mol/$m^3$ protected plants against arsenic toxicity in non-tolerant strains. Meharg & Macnair (1990) showed that arsenate tolerance in *H. lanatus* was due to an altered phosphate and arsenate uptake system, where the high-affinity uptake system is suppressed or absent in tolerant plants. Similar mechanisms of tolerance have been identified in the grasses *Deschampsia cespitosa* and *Agrostis capillaris* (Meharg & Macnair, 1991a).

#### 9.1.3.2 Invertebrates

Goldstein & Babich (1989) report arsenite and arsenate 7-day $LC_{50}$ values of 40.5 mg As(III)/kg (0.54 mmol/litre) and 59.3 mg As(V)/kg (0.79 mmol/litre) for the fruit fly *Drosophila melanogaster*. The 48-h $LC_{50}$s for As(III) and As(V) in drinking-water were 80 and 110 mg/litre respectively for the house fly *Musca domestica*. In the cabbage looper moth (*Trichoplusia ni*) 48-h$LC_{50}$s were 320 mg As(III)/kg diet and 794 mg As(V)/kg diet (Zaman & Pardini, 1995). Robertson & McLean (1985) found the dietary $LC_{50}$ for $As_2O_3$ to sixth instar western spruce budworm (*Choristoneura occidentalis*) to be 1932 mg As(III)/kg.

Meharg et al. (1998) maintained earthworms (*Lumbricus terrestris*) in sandy loam soil dosed with arsenate concentrations ranging from 15 to 500 mg/kg (dry weight). The natural soil arsenic level was 1.2 mg/kg. A plot of the concentration causing 50% mortality ($LC_{50}$) with time showed a steep decline between 2 and 8 days with the $LC_{50}$ ranging from 400 to 100 mg/kg. In a second experiment toxicity was found to increase with depth of soil, with the 4-day $LC_{50}$ ranging from 300 mg/kg at a depth of 0–70 mm to < 100 mg/kg at 500–700 mm.

Vaughan & Greenslade (1998) investigated the effect of arsenite and arsenate on survival and reproduction in three species of Collembola (springtails). The $EC_{50}$ for inhibition of reproduction over a 28-day exposure of *Folsomia candida* by arsenite was 3 mg/kg, compared with 119 mg/kg for arsenate. This species was the most sensitive Collembola to arsenite, followed by *Proisotoma minuta* ($EC_{50}$ 4.4 mg/kg) and *Sinella communis* ($EC_{50}$ 9.9 mg/kg).

Watson et al. (1976) exposed fourth-instar nymphs of meadow katydids (*Conocephalus fasciatus*) to drinking-water containing arsenical compounds. They reported 7-day $LD_{50}$s for the organic arsenicals cacodylic acid and Phytar 560 of 12.1 and 1.3 mg As/litre respectively; 14-day values were 2.6 and 0.4 mg As/litre respectively. The inorganic $As_2O_3$ and arsenic pentoxide showed 7- and 14-day $LD_{50}$s of 3.1 and 1.2 mg As(III)/litre, and 4.5 and 1.5 mg As(V)/litre respectively.

Bertholf & Pilson (1941) found the median lethal dose for arsenate to honey bees to be 0.6 µg As(V)/bee. The authors found a decrease in toxicity with an increase in particle size. At a fine particle size (3 µm) the median lethal dose was 0.7 µg As/bee whereas a coarse particle size (28 µm) resulted in a median lethal dose of 1.3 µg/bee.

#### *9.1.3.3 Vertebrates*

Toxicity of arsenic to birds is summarized in Table 44. Signs of acute arsenite poisoning in birds include ataxia, asthenia, slowness, jerkiness, falling, hyporeactivity, fluffed feathers, ptosis, huddled position, loss of righting reflex, immobility and tetanic seizures (Hudson et al., 1984).

Table 44. Toxicity of As to birds

| Species | Age | Arsenical | Parameter | Concentration (mg As/kg) | Reference |
|---|---|---|---|---|---|
| Mallard | | | | | |
| *Anas platyryhnchos* | 3 mo. | Arsenite | $LD_{50}$[a] | 323 (149–699) | Hudson et al. (1984) |
| | 3–4 mo. | Silvisar 510* | $LD_{50}$ | > 2400 | Hudson et al. (1984) |
| California quail | | | | | |
| *Callipepla californica* | 9–12 mo. | Arsenite | $LD_{50}$ | 47.6 (34.3–66) | Hudson et al. (1984) |
| Pheasant | | | | | |
| *Phasianus colchicus* | 3–4 mo. | Arsenite | $LD_{50}$ | 386 (221–671) | Hudson et al. (1984) |
| Chukar | | | | | |
| *Alectoris chukar* | 4 mo. | Silvisar 510* | $LD_{50}$ | ≥ 2000 | Hudson et al. (1984) |
| Japanese quail | | | | | |
| *Coturnix coturnix japonica* | 14 days | MMA | 5-day $LC_{50}$[b] | > 5000 | Hill & Camardese (1986) |

[a] $LD_{50}$ expressed as mg/kg body weight (single oral dose)

[b] $LC_{50}$ expressed as mg/kg diet

Silvisar 510–54.3%, total As = 27.14% (DMA 46%, triethanolamine DMA 8.3%); MMA monomethylarsonic acid

Holcman & Stibilj (1997) fed Rhode Island Red hens on a diet containing up to 30 mg As(III)/kg (as $As_2O_3$) for 19 days. No significant effects were found on feed consumption, number of eggs per hen, body weight or average egg weight.

Haegele & Tucker (1974) dosed female mallards (*Anas platyrhynchos*) with a single oral dose of 100 mg sodium arsenite/kg body weight. Eggshell thickness was reduced within 3 days but had recovered to normal 5 days after dosing. The authors suggest that this temporary reduction in eggshell thickness could be caused by a decrease in food consumption; however, food consumption was not monitored during the test.

Camardese et al. (1990) fed mallard ducklings (*A. platyrhynchos*) on a diet containing 30, 100 or 300 mg As(V)/kg (as sodium arsenate) for 10 weeks. Arsenic accumulated significantly in brain and liver of ducklings fed 100 or 300 mg/kg but did not result in histopathological lesions. In a similar experiment Whitworth et al. (1991) found that the highest exposure concentration caused a significant increase in resting time and a significant decrease in time spent in alert behaviours. Ducklings on 300 mg As(V)/kg spent significantly more time under the heat lamp. Arsenate had no effect on feeding behaviour. No significant effect on survival or growth was observed in mallard ducklings fed on a diet containing 200 mg As(V)/kg (as sodium arsenate) for 4 weeks. However, ducklings maintained on a protein-restricted diet at the same arsenate dose showed significant reductions in survival and growth, and an increased incidence of histopathological lesions (Hoffman et al., 1992). Stanley et al. (1994) found that 400 mg As(V)/kg (as sodium arsenate) significantly reduced mallard duckling growth but did not affect survival rate.

Hudson et al. (1984) found the $LD_{50}$ for the mule deer (*Odocoileus hemionus*) to be > 320 mg/kg for the organic arsenical Silvisar 510 (Phytar 560).

Savabieasfahani et al. (1998) exposed cotton rats (*Sigmodon hispidus*) to 5 or 10 mg/litre sodium arsenite in drinking-water for 6 weeks. Food intake was significantly depressed at both dose levels. However, there was no significant dose-related effect of arsenite on organ weights or immune function.

## 9.2 Field observations

### 9.2.1 Microorganisms

Arsenic resistance is often found in microorganisms inhabiting arsenic-contaminated environments (see section 9.1.1.1).

### 9.2.2 Aquatic organisms

Crearley (1973) found several dead turtles around the margin of a ponded area near a manufacturing plant for arsenic-based cotton defoliants. The concentration of arsenic in the pondwater was 63 mg As/litre. The turtles appeared to have been blind before death, with the tissue of the eyelid and the nasal area appearing to be keratinized. Three of five live turtles collected downstream in the headwaters of Finfeather Lake (Bryan, Texas, USA) were blind; the arsenic concentration in the lake was 8.5 mg/litre. Sorensen et al. (1985) collected green sunfish (*L. cyanellus*) from Municipal Lake, Bryan, Texas (water concentration 13.6 mg As/litre). Cellular changes in hepatocytes of sunfish were compared with levels of arsenic in the liver. Significant increases were observed in the volumes occupied by necrotic and fibrous bodies as arsenic levels in the liver increased. The surface density of rough endoplasmic reticulum increased significantly with increasing arsenic concentrations.

### 9.2.3 Terrestrial organisms

#### 9.2.3.1 Plants

Injury symptoms on crop plants resulting from toxic quantities of arsenic in soils were noted in the 1930s, when it was found that young trees planted in old orchard soils that had been treated with organic arsenicals grew slowly and were stunted (Snyder, 1935). In addition to being stunted, young apple trees had leaf symptoms that indicated water-deficiency stress, which implied injury to the roots (NAS, 1977). Trappe et al. (1973) report that apple trees growing in soil contaminated from the earlier use of lead arsenate insecticide (300 mg As(V)/kg) were stunted and had badly stunted rootlets that were sparsely mycorrhizal. Trees growing in the same area in soil at < 50 mg As/kg showed healthy growth and vigorous rootlets that were intensely mycorrhizal.

Symptoms similar to those previously attributed to arsenic toxicity from the use of lead arsenate insecticide were reported by Aggett & Aspell (1980) for apple trees growing near a timber mill processing wood treated with copper chrome arsenate. Total inorganic soil arsenic, available soil arsenic, arsenic residues in leaves and observed symptoms decreased with increasing distance from the source of the contamination.

Woolson et al. (1971) studied the effect of 29 arsenic-contaminated soils on the growth of corn plants (*Z. mays*). A significant correlation was found between growth reduction and increasing arsenic concentration with a much better correlation with available arsenic than with total arsenic.

Wild (1974) notes an extensive flora present on arsenical mine spoils in Africa (arsenic levels < 30 g/kg) but did not determine if these species exhibited resistance. A wide range of arsenate plant tolerances have been demonstrated from the arsenate-contaminated regions of the world. These include species such as *Andropogon scoparius* (Rocovich & West, 1975), *Agrostis capillaris* (Porter & Peterson, 1977), *Plantago laceolata* (Pollard, 1980), *Holcus lanatus* (Meharg & Macnair, 1990, 1991b, 1992) and *Silene vulgaris* (Paliouris & Hutchinson, 1991). The mechanistic basis of such adaptations in grasses is discussed in section 9.1.3.1.

#### *9.2.3.2 Vertebrates*

Buck et al. (1976) reported two cases of arsenic toxicosis in domesticated animals. Seven animals in a herd of 75 cattle died and when analysed were found to contain arsenic concentrations in the liver and kidney of 12.8–18.2 and 42.5–60 mg/kg respectively. The animals were being raised on poor-quality hay with little other forage available; however, they were also found to have access to a container of herbicide containing sodium arsenite. In another case five horses died when fed on grass cuttings from a field which had been treated with a crabgrass control formulation (47% $As_2O_3$; 3.5% lead arsenate). Liver and kidney tissue contained arsenic levels of 21.6 and 21–24 mg/kg respectively. Hullinger et al. (1998) reported a case of arsenic toxicosis attributable to ingestion of ashes from burned posts which had been treated with an arsenic-containing preservative. Lack of normal salt supplementation to the herd was

conducive to pica-like behaviour and ingestion of toxic ashes. Seven cows from a herd of 37 developed diarrhoea, weakness, stumbling and prostration. Four of the affected cattle died within 48 h. Arsenic was detected in liver tissue at 4.2 mg/kg, in abomasal contents at 42 mg/kg and in rumen contents at 105 mg/kg.

The herbicidal properties of arsenic made its use as a tree-debarker an important factor in the wood pulp industry in the north-eastern USA in the 1940s and 1950s. Cook (1953) reported two cases in New York State (USA) in which approximately 10 white-tailed deer consumed fatal amounts of sodium arsenite that was used to debark pulp trees. Field studies by Boyce & Verme (1954) showed that 923–2770 mg of arsenic (as sodium arsenite) was lethal to deer when licked from the bark of treated trees. The authors also report that wildlife kills from arsenic poisoning in Michigan (USA) in 1952 amounted to five deer, four porcupines, and one rabbit on about 81 ha of commercially treated trees. The practice of debarking trees with arsenicals has been replaced by mechanical techniques.

Swiggart et al. (1972) reported that 11 white-tailed deer (*Odocoileus virginianus*) were found dead after the aerial application of arsenic acid (52.3% $As_2O_3$) for the control of Johnson grass (*Sorghum halapense*). Livers from five of the deer were analysed and found to contain arsenic concentrations ranging from 16.8 to 24.3 mg/kg. The authors state that the levels of arsenic found were sufficient to have killed the deer but that the herbicide was not registered for such a use and, therefore, the deaths were attributed to misuse of the pesticide.

# 10. EVALUATION OF HUMAN HEALTH RISKS AND EFFECTS ON THE ENVIRONMENT

## 10.1 Effects on human health

### *10.1.1 Acute effects*

Inorganic arsenic is acutely toxic and ingestion of large doses leads to gastrointestinal symptoms, disturbances of cardiovascular and central nervous system functions, multiorgan failure and eventually death. In survivors, bone marrow depression, haemolysis, hepatomegaly, melanosis, polyneuropathy and encephalopathy may be observed.

### *10.1.2 Vascular effects*

Several studies in Taiwan have demonstrated an association between arsenic ingestion and blackfoot disease (BFD), with clear exposure–response effects related to both the well-water arsenic levels and duration of use of arsenic-contaminated drinking-water. Preclinical cases have also been identified by Doppler ultrasound in formerly exposed individuals, suggesting that the effects of arsenic ingestion can persist after exposure has declined or ceased. Several other studies and case reports of subjects exposed to arsenic from many sources, in countries other than Taiwan, document an association with peripheral vascular alterations. However, the extreme form and high prevalence of BFD found in Taiwan has not been reported in other parts of the world, and contributing factors, such as malnutrition or other concurrent exposures, may play a role in the pathophysiology of the disease.

Hypertension is associated with long-term exposure to arsenic, but this evidence is limited to cross-sectional studies, one occupational and two environmental (Taiwan and Bangladesh), all three of which found elevations in blood pressure with arsenic exposure. The two environmental studies demonstrated exposure–response relationships. It should be noted that although hypertension is not a very important cause of death itself, it is a major risk factor for other vascular diseases.

Several studies in Taiwan show a relationship between arsenic exposure and mortality from cardiovascular diseases (CVD), including exposure–response relationships. Similar results have generally not been observed in other arsenic drinking-water studies or in a medicinal study, in all of which the exposure levels have been lower. In the occupational studies, mortality from arteriosclerosis and coronary heart disease was elevated in the latest report from the Tacoma cohort (USA), but no statistically significant increases for these effects have been found in the Ronnskar (Sweden) or Anaconda (USA) smelter cohorts. The study in Utah found an excess of mortality from hypertensive heart disease but there were only a small number of deaths.

Only very limited evidence exists for an association between arsenic exposure and cerebrovascular disease. Some of the Taiwanese studies have shown an elevated risk of death from cerebrovascular disease, but the data are inconsistent across studies and the elevations, where present, are small compared with those for CVD. Studies from other countries provide only very limited support for the Taiwanese findings, but exposure levels were considerably lower.

### 10.1.3 Diabetes mellitus

In Taiwan, the prevalence and mortality rates of diabetes mellitus were higher among the population of the BFD-endemic area. There was also an exposure–response relationship between cumulative arsenic exposure and the prevalence of diabetes mellitus. A similar exposure–response pattern was observed in a study in Bangladesh, where prevalence of keratosis was used as a surrogate for arsenic exposure. Two occupational studies found an association of borderline statistical significance between diabetes mellitus and exposure to arsenic.

### 10.1.4 Neurological effects

Although there is good evidence that acute arsenic poisoning causes neurological effects, especially in the peripheral nervous system, there is little evidence of neurological effects from long-term lower-level environmental or occupational exposure. The few published studies have suggested changes in peripheral nerve

function after arsenic exposure, but the studies have been limited by small numbers, different methods used to assess the end-points and co-exposure to other known neurotoxins.

### *10.1.5 Cancer of the lung, bladder, and kidney*

Studies in Taiwan, Chile and Argentina show consistently high mortality risks from lung, bladder and kidney cancer among populations exposed to arsenic via drinking-water. Where exposure–response relations have been studied, the risk of cancer for these sites increases with increasing exposure. Even when tobacco smoking has been considered, the exposure–response relationship remains.

Not all studies of populations exposed to arsenic have reported positive findings for increased lung, bladder and kidney cancer. Exposure in these studies have not been as high as those in Taiwan, Chile or Argentina, and the sample sizes of the study populations may not have provided the statistical power to detect increased risks.

Studies on populations occupationally exposed to arsenic, such as smelter workers, pesticide manufacturers and miners in many different countries, consistently demonstrate an excess lung cancer risk among the arsenic-exposed. Although all these groups are exposed to other chemicals in addition to arsenic, it is unlikely that some other common factor could explain the findings. The lung cancer risk increases with increasing arsenic exposure in all studies where exposure–response relationships have been investigated. Tobacco smoking has been investigated in several studies in two of the three main smelter cohorts, and was not found to be the cause of the increased lung cancer risk attributed to arsenic; however, it was found to be interactive with arsenic in increasing the lung cancer risk.

Risks of kidney or bladder cancer are not consistently elevated in studies among people occupationally exposed to arsenic. This difference between the occupational and environmental studies may reflect lower systemic concentrations of arsenic after inhalation exposure than after oral exposure.

It is difficult to determine the lowest arsenic drinking-water concentration at which increased risks of lung, bladder and kidney

cancer may be found. Most of the studies where these effects have been observed were conducted in Taiwan. The exposure categories of studies conducted in the BFD-endemic area in Taiwan have historically been rather broad (e.g. < 300 µg/litre, 300–600 µg/litre, and > 600 µg/litre). A recent paper on the BFD-endemic area in Taiwan, however, reported increased risks of bladder and lung cancer mortality in persons consuming drinking-water with arsenic concentrations < 50 µg/litre.[1]

In Argentina, significantly elevated bladder, lung and kidney cancer mortality were found in the high-exposure group where over 75% of the measurements of arsenic in drinking-water were higher than the detection limit of 40 µg/litre. For the measurements over the detection limit, the average concentration was 178 µg/litre, which can be taken as the lowest exposure where these effects are observed. Exposure concentrations were not provided for the low- or intermediate-exposure groups although bladder, lung and kidney cancer mortality were significantly elevated for men and lung cancer mortality was significantly elevated for women in the intermediate-exposure group. Thus the lowest exposure where elevated kidney cancer risk could be observed would have to be considerably lower than 178 µg/litre.

In a case–control study conducted in Chile, there was an exposure–response relationship for the risk of lung cancer over all exposure categories, and the increased risk was statistically significant at exposure strata of 30–50 µg/litre and above. In a case–control study in Finland, a statistically significantly elevated risk of bladder cancer was observed at ≥0.5–64 µg As/litre drinking-water

[1] While this EHC was in the press, a cohort study from north-eastern Taiwan (Chiou et al., 2001) also reported an exposure-dependent increase in the risk of bladder cancer in exposure categories 10–50, 50–100, and > 100 µg/litre, with relative risks of transitional cell carcinoma of 1.0, 1.9 (CI 0.1–32.5), 8.2 (0.7–99.1) and 15.3 (1.7–139.9). Unlike all earlier Taiwanese studies, this study used estimates of individual (rather than village average) drinking-water arsenic concentrations, and incidence rather than mortality as the end-point. Arsenic measurements in the well-water were performed using a hydride-generation atomic absorption method, and the results were adjusted for age, sex and cigarette smoking.

concentration but only when exposure was 3–9 years before diagnosis.

### *10.1.6 Cancer and precancerous lesions of the skin*

Arsenic ingestion in drinking-water has been shown to be associated with a high risk of skin cancer. Well-documented studies on skin cancer after arsenic ingestion from drinking-water have been conducted in several populations in different countries, the largest of which were in Taiwan. Association of exposure to arsenic with skin cancer has also been observed in studies on patients treated with arsenicals. An early study found an excess of skin cancer mortality after occupational exposure to arsenic, but this was not observed in other occupational studies of arsenic exposure.

The lowest arsenic drinking-water concentration where an increased risk of skin cancer could be observed is in the lowest exposure group in the exposed Taiwan population (i.e. < 300 µg/litre). It should be noted that this is a very broad exposure category and the lowest concentration associated with skin cancer could have been considerably lower.

The lowest arsenic drinking-water concentration where an elevated risk of arsenic-associated skin lesions (hyperpigmentation and/or keratosis) has been found can be estimated from the study in West Bengal to be less than 50 µg/litre.

### *10.1.7 Cancer at other sites*

In two partly overlapping studies in Taiwan, an elevated mortality from liver cancer was observed in relation to arsenic exposure from drinking-water. In one of the two studies in Chile, but not in the study in Argentina, such a relationship was observed.

Cancer at other sites in relation to arsenic exposure has been little studied outside Taiwan. The sites that have exhibited an elevated risk include oesophagus, stomach, small intestine, colon, nose, larynx, bone and prostate, as well as lymphoma and leukaemia. A study in the USA and another in Australia, neither of which showed a clear-cut increase in the risk of lung, bladder, or kidney cancer, showed moderately elevated mortality from cancer of the

prostate. The studies on occupational exposure of arsenic have not found any consistent relationship between exposure to arsenic and cancer at sites other than lung.

It cannot be stated with certainty that arsenic exposure causes cancer at sites other than lung, skin, kidney and bladder. It is apparent that if such a causality exists, the relative risk of cancer at such sites must be lower than that for the sites for which the causality has been demonstrated.

### 10.1.8 Reproductive toxicity

Several studies have examined a number of reproductive end-points in relation to arsenic exposure, and the results suggest elevations in fetal, neonatal and postnatal mortality, lowered birth weight, spontaneous abortions, stillbirths, pre-eclampsia and congenital malformations. However, there is no consistent evidence for any one particular end-point.

### 10.1.9 Genotoxicity

Genotoxicity studies in relation to arsenic exposure have included exposed and unexposed individuals from several populations and analyses have been based on various tissues, including blood, buccal and bladder cells as well as sections from tumour biopsies or Bowen's disease.

Even with some negative findings, the overall weight of evidence (Table 45) indicates that arsenic can cause clastogenic damage in different cell types, with different end-points, in exposed individuals. Clastogenic effects have also been observed in cells from cancer patients. Arsenic is thus clastogenic in humans *in vivo* However, no *HPRT* gene mutation was seen in the single study in lymphocytes or increases in *ras* or *p53* gene expression in cells from cancer or Bowen's disease patients with long-term exposure to arsenic, except for one study with increased *p53* expression in Bowen's disease patients with such exposure compared to patients without exposure.

Table 45. Genotoxicity studies after As exposure – weight of evidence approach

| Micronuclei | Sister chromatid exchanges | Chromosome aberrations | Aneuploidy | HPRT mutation | p53/ras expression |
|---|---|---|---|---|---|
| Urinary epithelial cells<br>+ (USA) | lymphocytes<br>+ (Argentina) | lymphocytes<br>–,+ (Mexico) | lymphocytes<br>+ (Argentina) | lymphocytes<br>– (Mexico) | – urothelial cancer patients (Taiwan) |
| + (Northern Chile) | – (Mexico) | + (Mexico) | | | – Bowen's disease (Taiwan) |
| + (Argentina) | – (Argentina) | ± (Finland) | | | + Bowen's disease (Taiwan) |
| Buccal cells | + Bowen's disease (Taiwan) | + cancer patients (Taiwan) | | | |
| – (USA) | – cancer patients, BFD (Taiwan) | | | | |
| + (Mexico) | | | | | |

### 10.1.10 Supporting data from experimental studies

Several animal carcinogenicity studies on arsenic have been carried out, but limitations such as high dose levels, limited time of exposure and limited number of animals make these inconclusive. However, in a recent study, exposure of female mice to arsenic in drinking-water was associated with increased incidence in tumours involving mainly lung, liver, gastrointestinal tract and skin. Inorganic arsenic did not induce point mutations in bacteria or in mammalian cells. However, arsenic can produce chromosomal aberrations *in-vitro*, affect methylation and repair of DNA, induce cell proliferation, transform cells, and promote tumours. One study has indicated that DMA may cause bladder cancer in male rats at high doses.

### 10.1.11 Conclusions

Arsenic exposure via drinking-water is causally related to cancer in the lungs, kidney, bladder and skin. Drinking-water arsenic concentrations of $\leq$50 µg/litre have been associated with increased risks of cancer in the bladder and lung. Precursors of skin cancer have been associated with drinking-water arsenic levels $\leq$ 50 µg/litre. Occupational exposure to airborne arsenic is causally related to cancer of the lung. Cumulative exposure to $\geq$0.75 mg/m$^3$ · year has been associated with an increased risk of cancer of the lung.

Arsenic is considered to be genotoxic in humans on the basis of clastogenicity in exposed individuals and findings *in vitro*.

Arsenic exposure via drinking-water induces PVD. Whether arsenic alone is sufficient to cause the extreme form of this disease, BFD, is not known.

Conclusions on the causality of the relationship between arsenic exposure and other health effects are less clear-cut. The evidence is strongest for hypertension and CVD, suggestive for diabetes and reproductive effects and weak for cerebrovascular disease, long-term neurological effects and cancer at sites other than lung, bladder, kidney and skin.

## 10.2 Evaluation of effects on the environment

### *10.2.1 Exposure*

Arsenic is continually cycled through all environmental compartments. Arsenic can be elevated to high levels in water and soil because of the underlying geology or geothermal activity. In the aquatic environment arsenic concentrations can also become elevated in some estuaries and in waters near heavy industrial or mining and mineral-processing areas. The highest concentrations of arsenic in soil tend to be associated with mining waste.

Mean total arsenic concentrations in air from remote and rural areas range from 0.02 to 4 ng/$m^3$. Mean total arsenic concentrations in urban areas range from 3 to about 200 ng/$m^3$; much higher concentrations (> 1000 ng/$m^3$) have been measured in the vicinity of industrial sources.

Reported concentrations of arsenic in surface waters are summarized in Fig. 6. Concentrations of arsenic in open ocean seawater are typically 1–2 µg/litre. Arsenic is widely distributed in surface freshwaters, and background concentrations in rivers and lakes are generally < 2 µg/litre except in areas with volcanic rock and sulfide mineral deposits. Mean arsenic concentrations of 500 µg/litre and a maximum of 25 mg/litre have been reported for geothermal waters. Enhanced arsenic levels of < 10 mg/litre have been reported near anthropogenic sources such as mining and agrochemical manufacture. Mean sediment arsenic concentrations range from 5 to 3000 mg/kg, with the higher levels occurring in areas of contamination.

Reported concentrations of arsenic in soils are summarized in Fig. 7. Background concentrations in soil tend to range from 1 to 40 mg/kg, with a mean value of 5 mg/kg. Naturally elevated levels of arsenic in soils may be associated with geological substrata such as sulfide ores. Anthropogenically contaminated soils can have concentrations of arsenic up to several percent.

Three major modes of arsenic biotransformation have been found to occur in the environment: redox transformation between arsenite and arsenate, reduction and methylation of inorganic arsenic

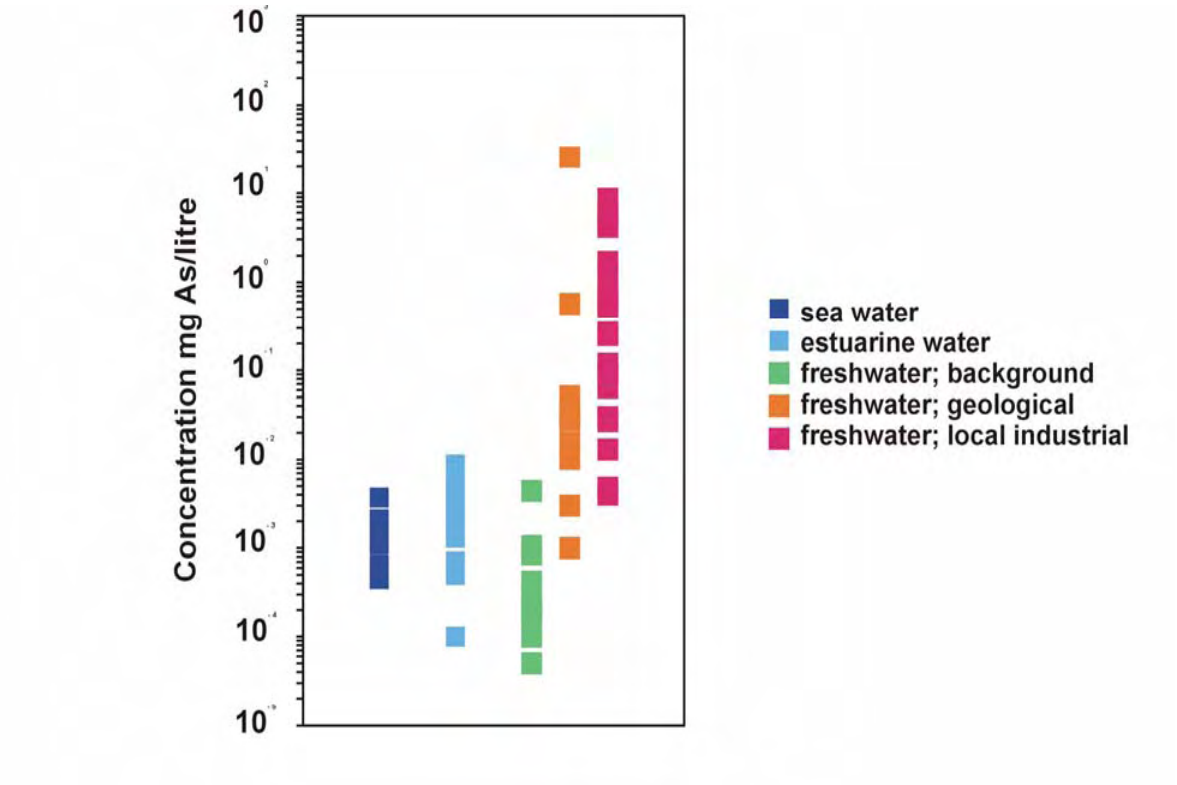


Fig 6. Reported concentrations of arsenic in seawater, estuarine water and freshwater. The seawater values will be background levels; some anthropogenic component is possible in estuarine concentration values. Freshwater values are separated into background (anthropogenic input unlikely), geological (volcanic/geothermal), and concentrations local to industrial activity (mining/agrochemical manufacture).

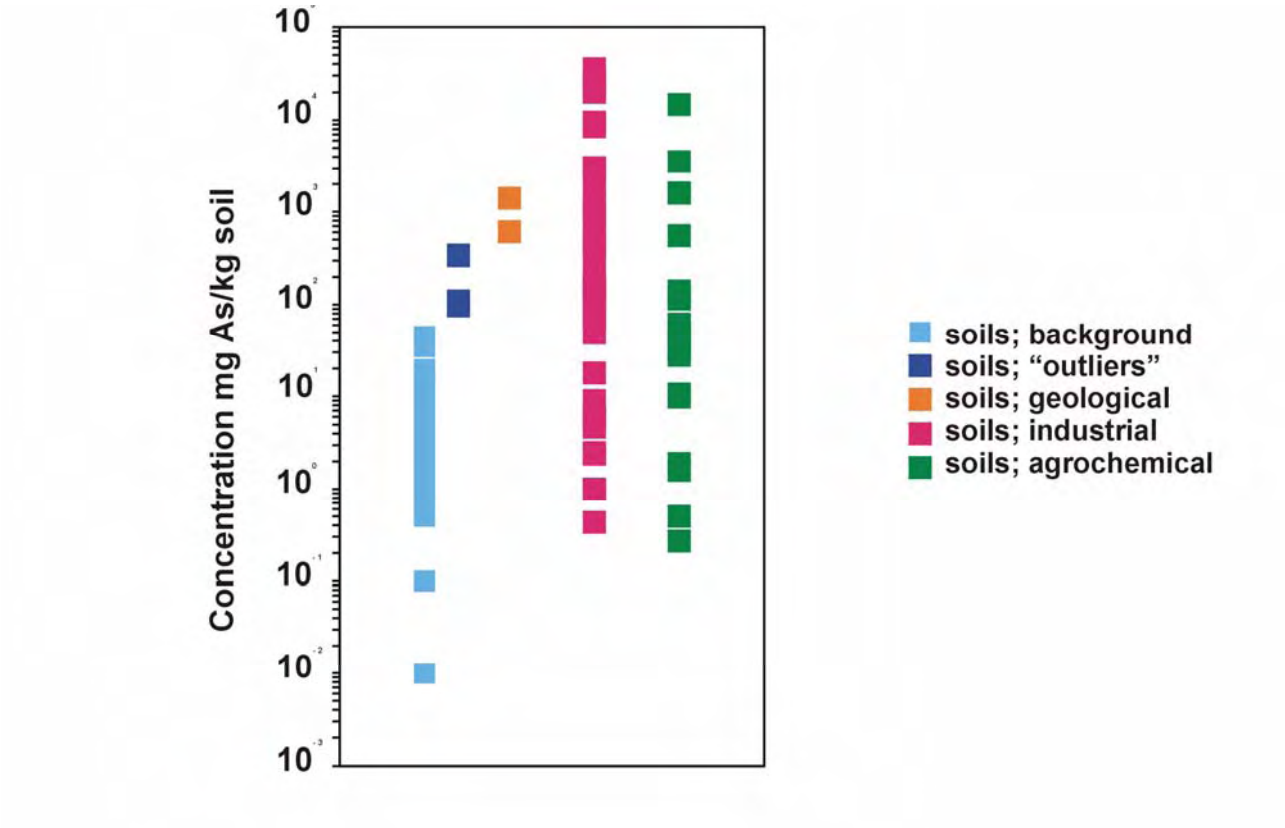


Fig 7. Reported concentrations of arsenic in soils. Values plotted as "outliers" are the upper end of ranges where bedrock or freshwater sediments were thought to contribute to higher than normal arsenic levels. "Geological" values are for volcanic areas. "Iindustrial" values include mining, smelting and manufacture of agrochemicals; the "agrochemicals" category covers concentrations following use of pesticides, sheep dips, etc.

and biosynthesis of more complex organic arsenic compounds. There is biogeochemical cycling of compounds formed from these processes. Bioaccumulation of organic arsenic compounds, after their biogenesis from inorganic forms, occurs in aquatic organisms. Biomagnification in aquatic food chains has not been observed. Terrestrial plants may accumulate inorganic arsenic by root uptake from the soil or by adsorption of airborne arsenic deposited on the leaves. Background arsenic concentrations in living organisms are usually < 1 mg/kg (fresh weight) in freshwater and terrestrial biota. These levels are higher in biota collected near anthropogenic sources or areas with geothermal activity. Marine organisms can normally contain much higher arsenic concentrations (< 100 mg/kg fresh weight) and these are predominantly organic arsenic species such as arsenosugars (macroalgae) and arsenobetaine (invertebrates and fish).

### 10.2.2 Effects

Aquatic and terrestrial biota show a wide range of sensitivities to the few arsenic species (inorganic arsenic and the simple methylated acids) that have been tested. Phytoplankton have generally been the most sensitive to inorganic arsenic (both arsenate and arsenite). Toxicity of inorganic arsenic in freshwater is summarized in Fig. 8. The lowest $EC_{50}$ value for growth in freshwater algae was at an arsenate concentration of 48 µg As/litre with a LOEC of 5 µg As/litre. NOECs for arsenite in 28-day tests on daphnids were between 600 and 1300 µg As/litre. In embryo-larval tests on fish and amphibians the lowest $LC_{50}$s for arsenate were 540 and 40 µg As/litre respectively. Toxicity of inorganic arsenic in seawater is summarized in Fig. 9. Adverse effects on marine periphyton communities were observed at arsenate concentrations of 15B60 µg/litre. For marine invertebrates the lowest acute $LC_{50}$s of arsenate for copepods were 10.9 (nauplius), 19.8 (copepodid) and 27.5 µg As/litre (ovigerous female). The toxicity of organic arsenic to aquatic organisms is summarized in Fig. 10.

Terrestrial toxicity of inorganic arsenic and organoarsenicals previously used as pesticides is summarized in Fig. 11. Levels of soil arsenic reported to be toxic to terrestrial plants span a broad range, with toxicity thresholds ranging from around 30 mg/kg to 300 mg/kg with toxicity tending to be greater in sandy than in clay soils. The

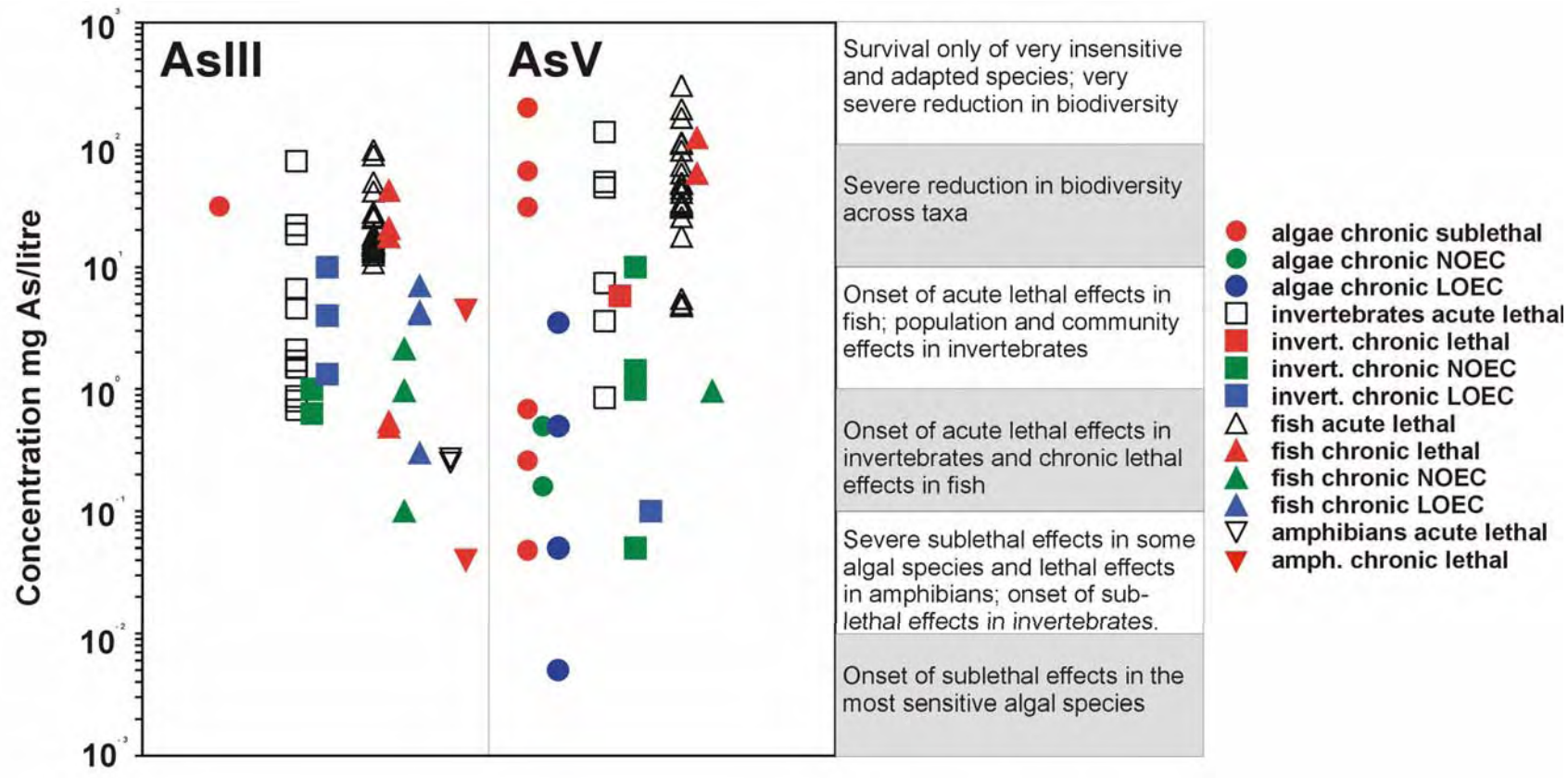


Fig 8. Acute and chronic effects of arsenite and arsenate in freshwater. Values are taken from the tables and text of Chapter 9. Likely effects are given for each order of magnitude increase in concentration. Effects assume no mitigation of toxicity in the environment.

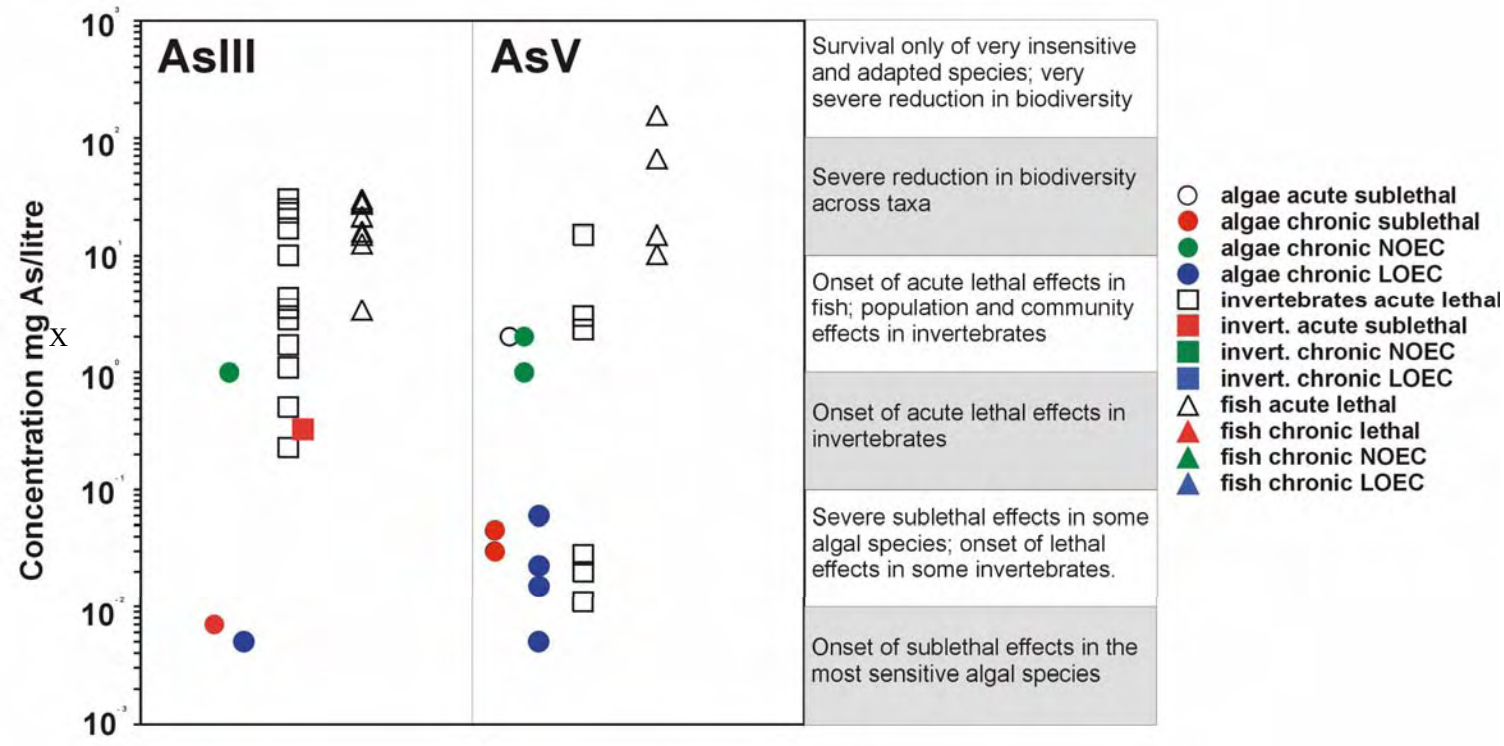


Fig 9. Acute and chronic effects of arsenite and arsenate in seawater. Values are taken from the tables and text of Chapter 9. Likely effects are given for each order of magnitude increase in concentration. Effects assume no mitigation of toxicity in the environment.

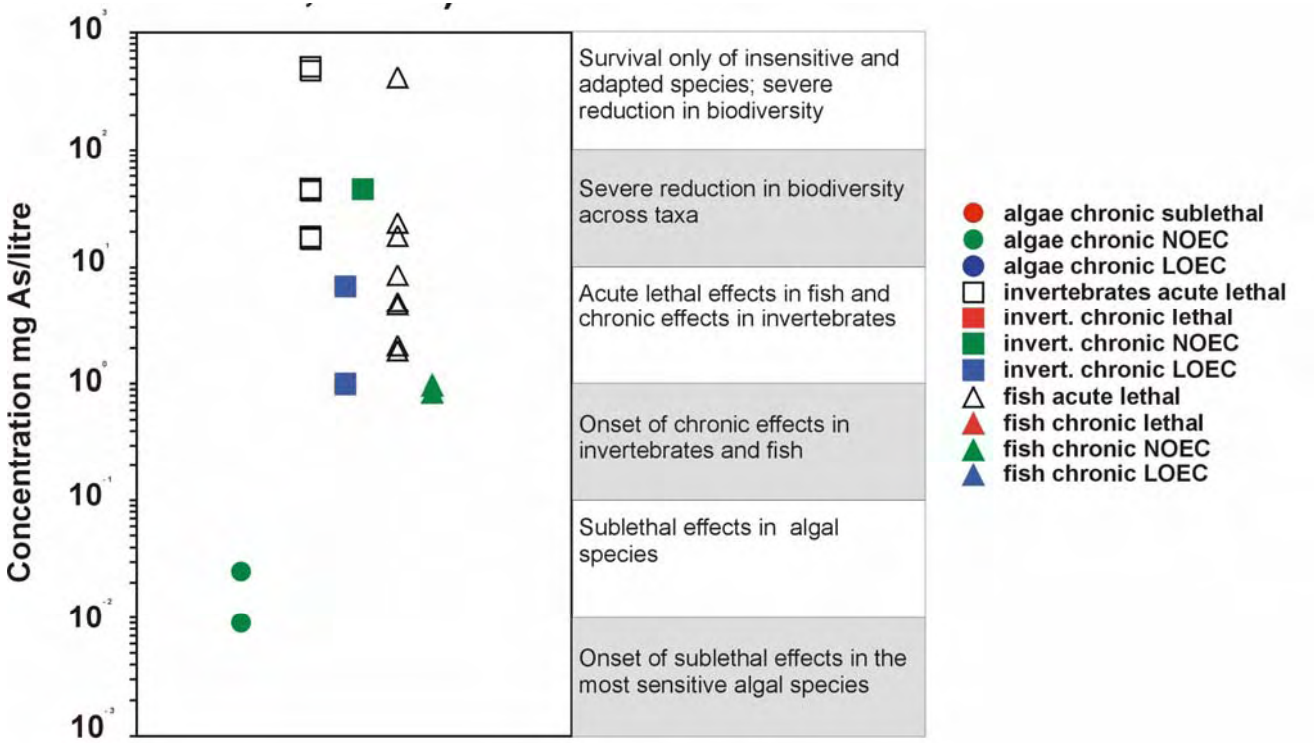


Fig 10. Acute and chronic effects of organic arsenic (monomethyl arsonic acid; MMA). Values are taken from the tables and text of Chapter 9. Likely effects are given for each order of magnitude increase in concentration. Effects assume no mitigation of toxicity in the environment.

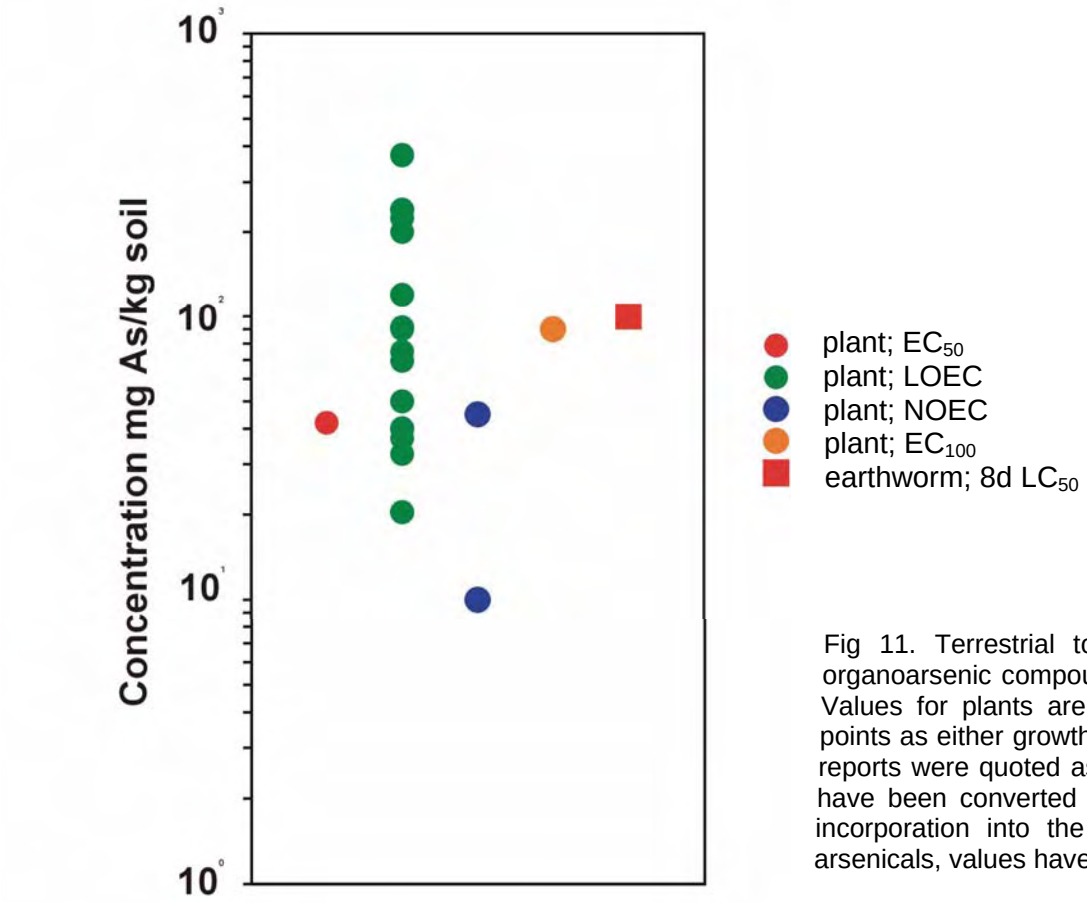


Fig 11. Terrestrial toxicity of inorganic arsenic and organoarsenic compounds formerly used as pesticides. Values for plants are sub-lethal effects with the end-points as either growth or yield. Where values in orginal reports were quoted as applicaton rates in kg/ha, these have been converted to mg/kg soil by assuming even incorporation into the top 5 cm of soil. For organic arsenicals, values have been recalcualted as As.

lowest critical plant tissue concentration was around 1 mg/kg. Very limited data are available for soil invertebrates. The only toxicity data available for birds are from acute, single-dose oral exposure which cannot easily be related to feeding exposure in the environment. Longer-term feeding studies with birds have not used doses which led to significant adverse effects; since all reported NOECs are "greater than" the highest experimental dose, values cannot be used for assessing risk.

### *10.2.3 Environmental modification of toxicity*

The figures summarizing aquatic toxicity list likely effects at differing concentrations of arsenic in surface waters. The suggested effects assume no mitigation of toxicity in the environment. In practice, the sensitivity of both aquatic and terrestrial organisms to arsenic is modified by biological and abiotic factors. In the environment arsenic toxicity is affected by temperature, pH, Eh, organic matter content, phosphate concentration, adsorption to solid matrices, and the presence of other substances and toxicants. In general, if the same organisms are compared under the same test conditions, then inorganic arsenicals are more toxic than the few pentavalent organic arsenic compounds likely to be encountered in the environment and arsenite is more toxic than arsenate. The mechanism of uptake of arsenate by organisms, and its mode of toxicity, differ considerably. This may explain some of the interspecies differences in response to different arsenic species. For example, the primary mechanism of arsenite toxicity is considered to result from its binding to protein sulfhydryl groups; arsenate is known to affect oxidative phosphorylation by competing with phosphate.

### *10.2.4 Risk evaluation*

Conventional, generic risk assessment would apply uncertainty factors to the lowest reported chronic effects concentration. For arsenic in freshwaters, this would be 5 µg/litre for growth in algae. This concentration is similar to the upper limit of the natural range of arsenic concentrations in most surface freshwaters. It is almost four orders of magnitude lower than the highest natural concentrations of arsenic in geothermal regions. Since communities of organisms occur in surface waters across the whole natural range

(0.05B25 000 µg/litre), a single protective concentration target for arsenic is inappropriate. Although there is no direct evidence that populations of organisms living at the higher end of the range for most surface waters (around 2 µg/litre) are less sensitive to arsenic than those at the bottom end of the range (0.05 µg/litre), this might be inferred from laboratory and field evidence. There is clear laboratory and field evidence that populations living at much higher concentrations have adapted to high inorganic arsenic levels. In addition, factors outlined above (section 10.2.3) may mitigate arsenic toxicity in the environment. Realistically, risk assessment for inorganic arsenic can only be done on a site-by-site basis taking into account background arsenic concentrations, local population tolerance and other local mitigating factors.

For populations of organisms living in low inorganic arsenic environments with little possible mitigation (e.g. low phosphate levels), a concentration of around 5 µg/litre would be protective of all but the most sensitive algae. Adapted populations at high natural inorganic arsenic concentrations will be specialized communities, possibly of lower biodiversity but probably of high conservation interest. Areas polluted by anthropogenic activity, therefore, present the risk manager with different options based on both practicability and desirability of remediation; if adapted communities have developed over time, these might be destroyed by remediation. Clearly the contamination of pristine areas with arsenic to levels which cause adaptation and decreased biodiversity is unacceptable.

From the limited data available for the marine environment it seems that inorganic arsenic concentrations in the open ocean do not overlap with reported toxic thresholds, suggesting minimal risk to organisms. The extreme sensitivity of some marine algae to inorganic arsenic is consistent with general low exposure and, therefore, no development of tolerance. Absorption of high concentrations of arsenate from ambient seawater by algae (accumulated as arsenosugars) may be linked to low phosphate levels. The reason for the accumulation of high concentrations of arsenobetaine in marine fish and invertebrates is uncertain. In estuaries, anthropogenic and geological sources may contribute to higher concentrations of arsenic which pose some risk to sensitive populations not previously exposed.

Reported total arsenic concentrations in soil can be very high. However, total arsenic is a poor indicator of toxicity to plants. Bioavailable arsenic represents a small percentage of total soil arsenic (10% or less and usually < 2%). Even with this low level of bioavailability, sensitive plants will be eliminated at some of the reported soil concentrations. On severely contaminated mine wastes, specialized plant communities tolerant to arsenic have developed. Some tolerant plants grow on wastes with total arsenic levels of several percent by weight. Communities are likely to be low in biodiversity at high arsenic concentrations.

Available data on soil invertebrates are very limited. Results for earthworms from one study suggest risk in soils with greater than background concentrations; the worms for this study were taken from soil low in arsenic. There is no published information on development of tolerance in soil invertebrate populations.

# 11. RECOMMENDATIONS FOR FUTURE RESEARCH

The Task Group identified the following areas where additional research might improve the assessment of risks to human health and environment induced by exposure to arsenic.

## 11.1 Human health

Better exposure–response epidemiological studies are required to characterize the potential health effects of arsenic at low levels of exposure, notably:

- longitudinal studies on cardiovascular morbidity, hypertension and diabetes
- epidemiological studies on reproductive end-points for which associations have already been suggested.
- longitudinal studies of neurological effects
- identification of sensitive subpopulations
- Influence of nutrition on arsenic metabolism and arsenic-induced effects
- biomarkers for arsenic exposure and health effects
- development of animal models for studying the carcinogenic and non-carcinogenic effects of arsenic
- better characterizations of the metabolism of arsenic, including formation of reactive intermediate metabolites, and possible genetic polymorphisms of the enzyme activities involved, and other factors influencing the metabolism
- mechanisms of action of the carcinogenic and non-carcinogenic effects of arsenic

- characterization of exposure to and bioavailability and toxicity of different arsenic species in foods, as well as variation in the levels of arsenic species in the same food items from different geographical areas

- development of robust, sensitive and accurate analytical techniques suitable for field measurements of arsenic in water and air.

## 11.2 Environmental

Further studies are required on:

- Global cycling and relative contributions of natural and anthropogenic sources of As.

- Concentrations and speciation in as well as effects of arsenic on zooplankton and phytoplankton in estuarine and marine ecosystems and freshwater aquatic systems.

- Concentrations of and possible effects of arsenic on terrestrial species.

- Metabolism of inorganic arsenic in algae, fish and shellfish.

# 12. PREVIOUS EVALUATIONS BY INTERNATIONAL BODIES

Arsenic and arsenic compounds were evaluated by the International Agency for Research on Cancer (IARC, 1973) and the evaluation updated in supplement 7 (IARC, 1987). There was *sufficient evidence* for carcinogenicity to humans and *limited evidence* for carcinogenicity to animals, and the overall evaluation was that arsenic and arsenic compounds are carcinogenic to humans (Group 1). This evaluation applies to the group of chemicals (i.e. arsenic and arsenic compounds) as a whole and not necessarily to all individual chemicals within the group.

The World Health Organization has given a provisional guideline value of 10 µg/litre for arsenic in drinking-water as the practical quantification limit (WHO, 1996).

The World Health Organization (WHO, 2000) has estimated that the unit risk for arsenic-induced lung cancer (risk estimate for lifetime exposure to a concentration of 1 $\mu g/m^3$) is $1.5 \times 10^{-3}$.

**LINKS TO THE OTHER SECTIONS OF THE DOCUMENT**