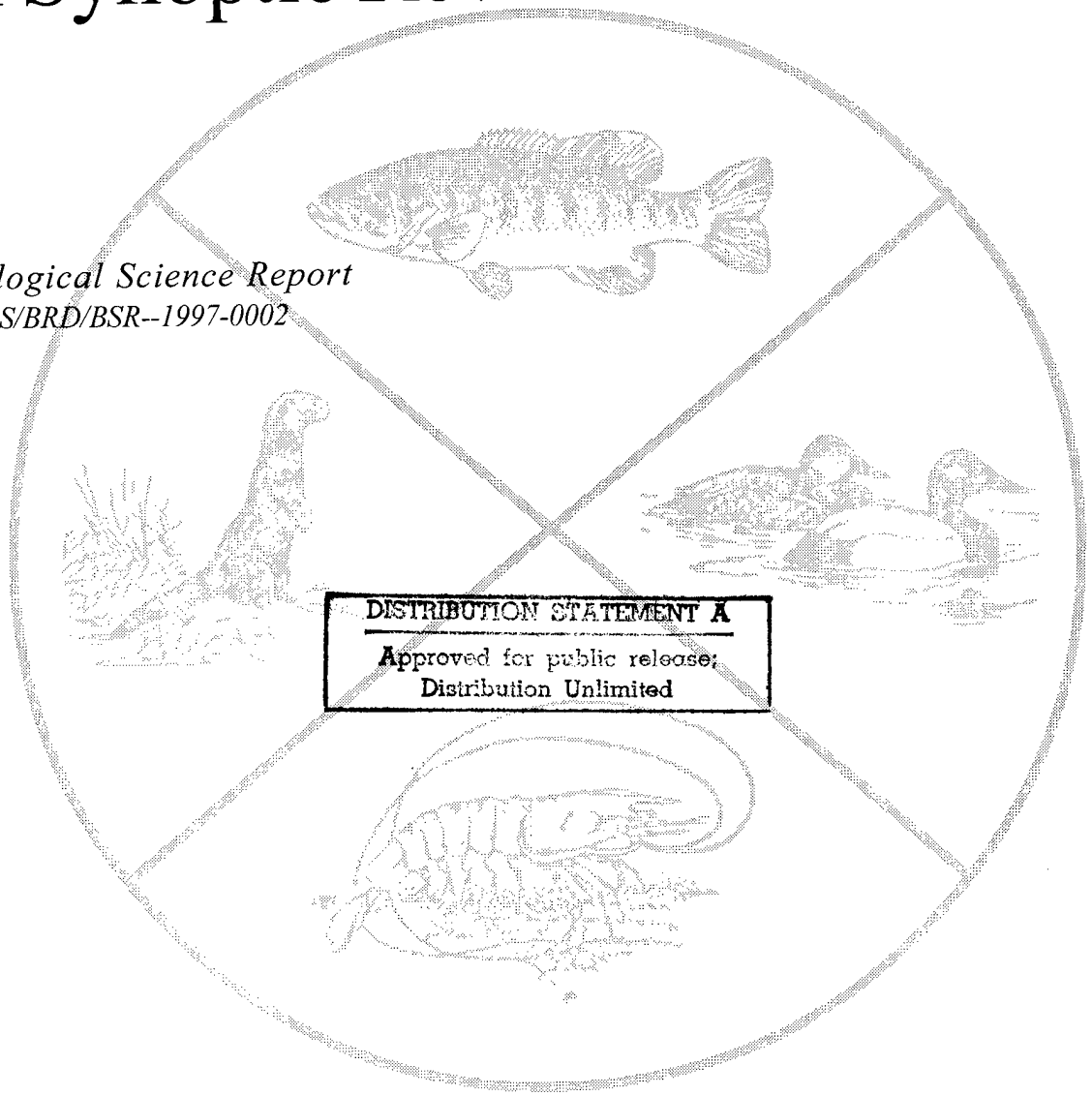
Copper Hazards to Fish, Wildlife, and Invertebrates:

A Synoptic Review

Biological Science Report
USGS/BRD/BSR--1997-0002



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This report is the first of the Contaminant Hazard Reviews to be published in the *Biological Science Report* series. Previous reports in the Contaminant Hazard Review series are listed on the inside back cover.

Biological Science Reports ISSN 1081-292X

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Information and Technology Reports ISSN 1081-2911

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Funding for printing this report was provided by the USGS/BRD Patuxent Wildlife Research Center, Laurel, MD. Production was by the USGS/BRD National Wetlands Research Center, Lafayette, LA (see inside back cover).

To purchase this report, contact the National Technical Information Service, 5285 Port Royal Road, Springfield, VA 22161 (call toll free 1-800-553-6847), or the Defense Technical Information Center, 8725 Kingman Rd., Suite 0944, Fort Belvoir, VA 22060-6218.

Errata Sheet for USGS/BRD/BSR 1997-0002

The suggested citation on page *ii* should read:

Eisler, R. 1998. Copper hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Geological Survey, Biological Resources Division, Biological Science Report USGS/BRD/BSR--1997-0002. 98 pp.

REPORT DOCUMENTATION PAGE

Form approved
OMB No. 0704-0188

1. AGENCY USE ONLY (Leave Blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	January 1998	Final

4. TITLE AND SUBTITLE

Copper Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review

5. FUNDING NUMBERS

6. AUTHOR(S)

R. Eisler

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESSES

U.S. Department of the Interior
U.S. Geological Survey/Biological Resources Division
Patuxent Wildlife Research Center
Laurel, Maryland 20708

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESSES

U.S. Department of the Interior
U.S. Geological Survey/Biological Resources Division
Washington, D.C. 20240

10. SPONSORING, MONITORING AGENCY REPORT NUMBER

Biological Science Report
USGS/BRD/BSR--1997-0002

11. SUPPLEMENTARY NOTES

Internally numbered as Contaminant Hazard Review Report 33

Errata sheet added for page ii.

12a. DISTRIBUTION/AVAILABILITY STATEMENT

Release unlimited. Available from the National Technical information Service, 5285 Port Royal Road, Springfield, VA 221261 (1-800-553-6847 or 703-487-4650). Available to registered users from the Defense Technical Information Center, Attn: Help Desk, 8725 Kingman Road, Suite 0944, Fort Belvoir, VA 22060-6218 (1-800-225-3842 or 703-767-9050)

12b. DISTRIBUTION CODE

13. ABSTRACT (Maximum 200 words)

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14. SUBJECT TERMS (Keywords)

Copper, copper sulfate, metals, toxicity, deficiency, criteria, residues, agriculture, nutrition, metallothionein, fish, invertebrates, amphibians, birds, wildlife, livestock, endangered species

15. NUMBER OF PAGES

iv + 98 pp

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	

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Biological Science Report
USGS/BRD/BSR--1997-0002
January 1998

Contaminant Hazard Reviews Report 33

By

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Suggested citation:

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Copper Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review

by

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Abstract. This report is a selective review and synthesis of the technical literature on copper and copper salts in the environment and their effects primarily on fishes, birds, mammals, terrestrial and aquatic invertebrates, and other natural resources. The subtopics include copper sources and uses; chemical and biochemical properties; concentrations of copper in field collections of abiotic materials and living organisms; effects of copper deficiency; lethal and sublethal effects on terrestrial plants and invertebrates, aquatic organisms, birds, and mammals, including effects on survival, growth, reproduction, behavior, metabolism, carcinogenicity, mutagenicity, and teratogenicity; proposed criteria for the protection of human health and sensitive natural resources; and recommendations for additional research.

Key words: Copper, copper sulfate, metals, toxicity, deficiency, criteria, residues, agriculture, nutrition, metallothionein, fish, invertebrates, amphibians, birds, wildlife, livestock, endangered species.

Copper (Cu) is plentiful in the environment and essential for the normal growth and metabolism of all living organisms (Schroeder et al. 1966; Carbonell and Tarazona 1994). Abnormal levels of copper intake may range from levels so low as to induce a nutritional deficiency to levels so high as to be acutely toxic (U.S. Environmental Protection Agency [USEPA] 1980). Copper is probably the first metal worked by humans some 70 to 80 centuries ago (Schroeder et al. 1966). The earliest known artifacts of hammered copper date from about 6000 BCE. After 4000 BCE, melting and casting of copper was common in the Near East. Smelting was developed about 3000 BCE and bronze around 2500 BCE. Brass, a copper alloy, was developed in Roman times. Copper derives from the Latin *cuprum*, a corruption of *cyprium*, Cyprus being the source of Egyptian and Roman copper (Schroeder et al. 1966). Copper was identified in terrestrial plants in 1817 (Gallagher 1979), in marine invertebrates in 1833 (Schroeder et al. 1966), in vertebrates in 1838 (Gallagher 1979), and in hemocyanin—the blue respiratory pigment of mollusks and crustaceans—in 1880 (Schroeder et al. 1966). But the metabolic importance of copper in plants and animals was not suspected until the 1920's when diseases due to copper deficiency began to be recognized (National Academy of Sciences [NAS] 1977; Gallagher 1979). Copper deficiency in vertebrates, for example, is associated with anemia, gastrointestinal disturbances, aortic aneurisms, bone development abnormalities, and death (Aaseth and Norseth 1986).

Copper toxicosis in terrestrial higher plants is rare but occurs on mine spoils and where copper-rich manures or fungicides are used excessively (Schroeder et al. 1966; NAS 1977; Alva et al. 1995; Arduini et al. 1995). Copper is among the most toxic of the heavy metals in freshwater and marine biota (Schroeder et al. 1966; Betzer and Yevich 1975), and often accumulates and causes irreversible harm to some species at concentrations just above levels required for growth and reproduction (Hall et al. 1988). Birds and mammals, when compared to lower forms, are relatively resistant to copper. But diets containing elevated concentrations of copper are sometimes fatal to ducklings (Wood and Worden 1973) and livestock when fed for extended periods. Domestic sheep (*Ovis aries*) are the most susceptible farm animals to chronic copper poisoning and effects include liver damage, impaired reproduction, reduced resistance to diseases, jaundice, and death (Gopinath and Howell 1975; Higgins 1981; Bires et al. 1993).

Many reviews and annotated bibliographies are available on copper ecology and toxicology, including those by Eisler (1973, 1979), Eisler and Wapner (1975), NAS (1977), Eisler et al. (1978, 1979), Nriagu (1979a, 1979b), USEPA (1980), Aaseth and Norseth (1986), and Agency for Toxic Substances and Disease Registry [ATSDR] (1990). I prepared this report at the request of resource contaminant specialists of the U.S. Fish and Wildlife Service; it is part of a continuing series of synoptic reviews on contaminant hazards to natural resources.

Sources and Uses

General

The United States is the major world producer and consumer of copper and its compounds. Most of the copper produced is used to manufacture electrical equipment, pipe, and machinery. Copper releases to the global biosphere—which may approach 1.8 million metric tons per year—come mostly from anthropogenic activities such as mining and smelting, industrial emissions and effluents, and municipal wastes and sewage sludge. Copper compounds are widely used as biocides to control nuisance algae and macrophytes, freshwater snails that may harbor schistosomiasis and other diseases, ectoparasites of fish and mammals, marine fouling organisms, and mildew and other diseases of terrestrial crop plants. Copper compounds are also used in agricultural fertilizers, in veterinary and medical products, in the food industry, and as a preservative of wood and other materials.

Sources

Global copper production during the past 60 centuries is estimated at 307 million metric tons, most of which (79%) occurred since 1900; annual global production of copper is now estimated at 13.6 million tons (Nriagu 1979c). Copper occurs naturally in many minerals and as uncombined metal. The three most important sources of copper are chalcocite (Cu_2S), chalcopyrite ($CuFeS_2$), and malachite ($CuCO_3 \cdot Cu(OH)_2$; ATSDR 1990).

The United States is the largest global consumer and producer of copper. In 1986, domestic consumption of copper in the United States was 2.14 million metric tons and mine production was 1.14 million metric tons, mostly from mines in Arizona, New Mexico, and Michigan. The major copper deposits in the United States are of hydrothermal origin and uniformly distributed in fractures or veins (ATSDR 1990). Copper is the major toxic component in streams impacted by active placer mines (Buhl and Hamilton 1990). About 60% of copper metal is eventually recycled; in 1986, smelting of scrap copper produced an additional 0.9 million metric tons of copper. Also in 1986, 1.1 million tons of copper were imported into the United States, mostly from Canada, Chile, Peru, and Mexico (ATSDR 1990).

The amount of copper entering the global ecosystem annually is unknown, but estimates range from 211,000 metric tons (Nriagu 1979c) to 1.8 million metric tons (NAS 1977). About 80.7% of this copper is deposited in terrestrial compartments, 15.7% in the hydrosphere, and 3.6% to the atmosphere (Nriagu 1979c). The residence time for copper in the deep ocean is 1,500 years; in soils it may be retained for as long as 1,000 years; in air, copper persists for about 13 days (Nriagu 1979c). Copper in the atmosphere results mainly (73%) from human activities such as copper production and combustion of fossil fuels; the remainder is from natural sources that include seasalt sprays, windblown dusts, volcanogenic particles, and decaying vegetation (Nriagu 1979c, 1979d).

Input of copper into aquatic ecosystems increased sharply during the past century and includes inputs from waste discharges into saline waters, industrial discharges into freshwater, and leaching of antifouling marine paints and wood preservatives (Nriagu 1979c). Present anthropogenic inputs of copper are two to five times higher than natural loadings; the atmosphere is a primary recipient of these inputs (Nriagu 1979d). In mining and industrial areas, precipitation of atmospheric fallout is a significant source of copper to the aquatic environment (USEPA 1980). More than 99.9% of oceanic copper fell as clay and manganese oxide particles in precipitation (NAS 1977). In the lower Great Lakes, direct atmospheric inputs of copper—in metric tons per year—range from 55 to 2,300 for Lake Michigan, 120 to 330 for Lake Erie, and 72 to 123 for Lake Ontario; regional disparities in atmospheric deposition of copper are related to the intensity of industrial activity and to the regional wind systems (Nriagu 1979d).

Copper in soils may come from a variety of anthropogenic sources: mining and smelting activities; other industrial emissions and effluents; traffic; fly ash; dumped waste materials; contaminated dusts and rainfall; sewage and sludge; pig slurry; composted refuse; and agricultural fertilizers, pesticides, and fungicides (Nriagu 1979c; Thornton 1979; Ma 1984; ATSDR 1990; Roncero et al. 1992; Alva et al. 1995). In the case of Florida citrus groves, copper-containing fertilizers applied during the early 1900's accounted for as much as 34 kg Cu/ha annually, and routine fungicidal sprays contributed another 10 kg Cu/ha annually. Surface soils (0-15 cm) from some mature citrus groves contained as much as 540 kg Cu/ha (Alva et al. 1995). Copper deposition rates in soils are higher in cities and near highways, railroads, power plants, and industrial activities (Nriagu 1979d). But a Kansas landfill near a freshwater stream had no significant effect on copper concentrations in water, sediments, crayfish, and sunfish (Morrissey and Edds 1994).

Uses

Metallic copper end uses include electrical (70%), construction (15%), machinery (6%), transportation (4%), and

ordinance (2%). The top domestic markets for copper and its alloys in 1986 were, in order of importance, plumbing, building wire, telecommunications, power utilities, in-plant equipment, air conditioning, automotive electrical, automotive nonelectrical, business electronics, and industrial valves and fittings (ATSDR 1990). A small percentage of copper production is used to manufacture chemicals, mainly copper sulfate. Of the copper sulfate used domestically, 65% is used in agriculture for fungicides, algicides, nutritional supplements, insecticides, and repellents; 28% is used industrially in froth flotation production of chromated copper arsenate wood preservatives, in electroplating, and in the manufacture of azo dyes; and 7% is used in water treatment to control nuisance algae (ATSDR 1990).

Copper is widely used to control unwanted species of freshwater algae and macrophytes (Bartley 1967; NAS 1977; USEPA 1980; Rowe and Prince 1983; Havens 1994). Chelated copper products are claimed to be effective algicides in hard water; the chelation of copper by organic compounds, such as ethanolamines or ethanolamine complexes, protects copper from precipitation and complexation (Straus and Tucker 1993). Copper sulfate is approved by the U.S. Environmental Protection Agency (USEPA) as an algicide in waters used to raise fish for human consumption (Straus and Tucker 1993). In algae, copper inhibits photosynthesis, nitrogen fixation, and phosphorus uptake; it selectively eliminates cryptophytes but spares diatoms (Havens 1994). Copper sulfate at low concentrations has been used to control freshwater algae in Wisconsin since 1918 without any conclusively proven effect on diversity or abundance of nontarget species (Mackenthun and Cooley 1952). But reduced abundance of freshwater benthos was noted in Lake Monova, Wisconsin, which received 771 metric tons of copper to control algae over a 26-year period and had sediment levels as high as 1,093 mg Cu/kg DW (Mackenthun and Cooley 1952). Copper sulfate used to control algal blooms in Wisconsin lakes at 1.25 mg Cu/L killed nontarget fishes, crustaceans, snails, and amphibians in 14 days or less; however, 0.25 mg Cu/L was not fatal to these species in 20 days (Hasler 1949). Concentrations as low as 0.03 mg Cu/L inhibited growth in two of four species of nuisance aquatic weeds in Lake Mendota, Wisconsin, and 0.3 mg Cu/L was fatal to all four species (Hasler 1949). Copper sulfate controls algae in cranberry bogs at 0.4 mg Cu/L but this concentration also kills resident fishes (Deubert and Demoranville 1970). Copper was not measurable in the surface waters of cranberry bogs within 10 days of treatment, regardless of initial copper concentration; it is probable that copper was adsorbed onto bog soils (Deubert and Demoranville 1970). In England, copper sulfate was effective at 1.0 mg Cu/L in controlling algae and most species of aquatic weeds for 1.6 km downstream of treatment for 6 months during the summer; only 0.25 mg Cu/L was necessary in autumn and winter for effective aquatic weed control (Chancellor et al. 1960). During copper treatment to control plants, aquatic snails were greatly reduced or eliminated but fishes seemed unaffected. Sensitive aquatic weeds included *Myriophyllum spicatum*, *Elodea canadensis*, *Potamogeton* spp., and *Lemna minor*; sensitive genera of algae included *Oedogonium*, *Spirogyra*, *Enteromorpha*, and *Mougeotia* (Chancellor et al. 1960).

In Iowa lakes, copper sulfate was used to control summer blooms of various species of toxic blue-green algae. Prior to treatment, blooms of *Anabaena flos-aquae*, *Aphanizomenon flos-aquae*, and *Microcystis aeruginosa* were associated with deaths of migratory waterfowl, game birds, songbirds, game, and domestic animals (Rose 1954). Most of these species of algae were controlled within 24 h by 1.0 mg Cu/L as copper sulfate. Copper treatment had no adverse effects on bottom fauna but populations of crustaceans (daphnids, copepods, entomostracans) were reduced. One year after treatment no deaths of birds or mammals were recorded (Rose 1954).

Copper salts are intentionally added to drinking water supplies of some municipalities to control growth of algae; concentrations as high as 59 µg Cu/L are maintained in New York City (USEPA 1980).

Copper compounds are used routinely and widely to control freshwater snails that serve as intermediate vectors of schistosomiasis and other diseases that afflict humans (Hasler 1949; NAS 1977; Rowe and Prince 1983; Winger et al. 1984; Al-Sabri et al. 1993). These compounds include copper sulfate, copper pentachlorophenate, copper carbonate, copper-tartaric acid, Paris green (copper arsenite-acetate), copper oxide, copper chloride, copper acetyl acetonate, copper dimethyl dithiocarbamate, copper ricinoleate, and copper rosinate (Cheng 1979). Also, many species of oyster enemies are controlled by copper sulfate dips. All tested species of marine gastropods, tunicates, echinoderms, and crabs that had been dipped for 5 seconds in a saturated solution of copper sulfate died if held in air for as little as a few seconds to 8 h; mussels, however, were resistant (MacKenzie 1961).

Copper sulfate is used to control protozoan fish ectoparasites including *Ichthyopthirius*, *Trichodina*, and *Costia*; the effectiveness of the treatment diminishes with increasing total alkalinity and total hardness of the water (Straus and Tucker 1993). Copper compounds now used to control protozoan parasites of cultured red drum (*Sciaenops ocellatus*) include copper sulfate, copper sulfate plus citric acid, and chelated copper compounds (forms of copper bound by sequestering agents, such as ethanolamine); chelated copper compounds are considered less toxic to fish than copper sulfate and at least as effective in controlling parasites (Peppard et al. 1991).

Copper is the active agent in many antifouling paints applied to watercraft (Aaseth and Norseth 1986; Hall et al.

1988). The growing use of copper-based paints subsequent to the prohibition in 1982 of tributyltin-based paints (Hall et al. 1988) is associated with elevated copper concentrations in Pacific oysters (*Crassostrea gigas*) farmed in the Bay of Arcachon, France (Claisse and Alzieu 1993).

Copper compounds are used in agriculture to treat mildew and other plant diseases; in the food industry as preservatives, additives, or coloring agents; in preservatives of wood, leather, and fabrics; in coin manufacture; and in water treatment (ATSDR 1990; Roncero et al. 1992). The use of copper-containing pesticides is traditional along the Mediterranean Coast, especially the use of Bordeaux mixture, a copper sulfate-based fungicide that has been widely used for more than a century to prevent mildew on grape vines (Romeu-Moreno et al. 1994). However, at current application rates of about 0.8 mg Cu/cm^2, Bordeaux mixture significantly reduces the life span and breeding rate of the fruit fly (*Drosophila melanogaster*) (Marchal-Segault et al. 1991).

Copper is widely used in veterinary clinics in medical products (Roncero et al. 1992). Copper sulfate is used by veterinarians to treat cattle and sheep for helminthiasis and infectious pododermatitis (NAS 1977). Cuprol (a 1% solution of cupric oleinate) is used to control lice (Aaseth and Norseth 1986). Copper is routinely used as a growth supplement in the diets of swine (*Sus* sp.) in the United Kingdom and elsewhere; diets may contain as much as 250 mg Cu/kg ration (USEPA 1980). The intensity of pig farming within about 10 km from the coast may influence copper content in estuarine sediments. For example, intensive pig farming in coastal Brittany, France, increased soil copper concentrations by 0.6 kg/ha annually and increased coastal sediment copper concentrations to as high as 49.6 mg/kg DW (Arzul and Maguer 1990).

In human medicine, metallic copper is used in some intrauterine devices, and various copper compounds are used as emetics and to treat rheumatoid arthritis (USEPA 1980; Aaseth and Norseth 1986). Some individuals wear copper bracelets as treatment for arthritis although its therapeutic value has little support (USEPA 1980).

Chemical and Biochemical Properties

General

This section demonstrates that (1) free ionic copper (Cu^{2+}) is the most toxic chemical species of copper and that copper bioavailability is modified by many biological and abiotic variables; (2) copper metabolism and sensitivity to copper of poikilotherms differs from that of mammals; and (3) copper interactions with inorganic and organic chemicals are substantial and must be considered when evaluating copper hazards to natural resources.

Chemical Properties

Copper is a soft heavy metal, atomic number 29, with a density in elemental form at 20° C of 8.92 g/cc and a melting point of 1,083.4° C (USEPA 1980; Aaseth and Norseth 1986; Table 1). Copper has two natural isotopes: Cu-63 (69.09%) and Cu-65 (30.91%; NAS 1977).

Copper exists in four oxidation states: Cu^0, Cu^{+1}, Cu^{+2}, and Cu^{+3} (ATSDR 1990). Elemental copper (Cu^0) is readily attacked by organic and mineral acids that contain an oxidizing agent and is slowly soluble in dilute ammonia; halogens attack elemental copper slowly at room temperature to yield the corresponding copper halide (USEPA 1980);

Table 1. Some properties of copper and copper sulfate (ATSDR 1990).

Property	Copper	Copper sulfate
Chemical and other names	Copper	Cupric sulfate, blue vitriol, cupric sulphate, Roman vitriol, Salzburg vitriol, blue copperas, copper (II) sulfate
Chemical formula	Cu	$CuSO_4$
Oxidation state	0	2+
CAS (Chemical Abstract Services) number	7440-50-8	7758-98-7
Molecular weight	63.546	159.60
Color and form	Reddish solid	Blue crystals
Melting point	1,083.4° C	Decomposes slightly at >200° C
Boiling point	2,567° C	Decomposes to CuO at 650° C
Density	8.92	3.603
Solubility		
Water	Insoluble	143 g/L
Organic solvents	Insoluble	Soluble in methanol, slightly soluble in ethanol

elemental copper is not oxidized in water (Aaseth and Norseth 1986). Cuprous copper (Cu^{+1}) exists only in water solution when complexed, usually in a tetrahedral form, with affinity for sulfur and nitrogen ligands (Schroeder et al. 1966). Cuprous copper is unstable in aerated aqueous solution over the pH range 6 to 8, and will undergo auto-oxidation-reduction into elemental copper (Cu^0) and cupric ion (Cu^{+2}) (USEPA 1980; Aaseth and Norseth 1986). The only cuprous ion (Cu^{+1}) compounds that are stable in water are extremely insoluble ones such as cuprous chloride (CuCl; ATSDR 1990). Cuprous ion-complexes may be formed in seawater by photochemical processes and persist for several hours. The cupric ion (Cu^{+2}) is the one generally encountered in water. Cupric ions are coordinated with six water molecules in solution (ATSDR 1990). Cupric ion ordinarily forms planar, less stable chelates with nitrogen and oxygen ligands (Schroeder et al. 1966). In seawater and sediment interstitial waters, the free cupric ion (Cu^{+2}) is the most readily available and toxic inorganic species of copper; however, the free ion concentration is sensitive to complexation and is less available to aquatic biota in the presence of natural organic chelators and high salinities (Bryan and Langston 1992). Cupric ions account for about 1% of the total dissolved copper in seawater and less than 1% in freshwater (Boyle 1979). Trivalent copper (Cu^{+3}) probably does not occur naturally (Schroeder et al. 1966). Trivalent copper is strongly oxidizing and occurs only in a few compounds; none of these compounds is currently considered industrially important or environmentally significant (ATSDR 1990).

Copper speciation in freshwater is figured in detail by Leckie and Davis (1979). In freshwater, the solubility of copper salts is decreased under reducing conditions and is further modified by water pH, temperature, and hardness; size and density of suspended materials; rates of coagulation and sedimentation of particulates; and concentration of dissolved organics. The chemical form of copper in freshwater is important in controlling geochemical and biological processes. But the lack of knowledge on the adsorption characteristics of most cupric ion (Cu^{+2}) complexes contributes to uncertainties about the behavior of known copper species (Leckie and Davis 1979). Ionic copper (Cu^{+2}) and some copper hydroxyl species are correlated with high toxicity to aquatic life; however, carbonato species ($CuHCO_3^+$, $CuCO_3$, $Cu(CO_3)_2^{-2}$) are much less toxic than other copper complexes (Meador 1991). The major chemical species of copper in freshwater are $Cu(CO_3)_2^{-2}$ and $CuCO_3$ (Boyle 1979). Cupric ion is the dominant toxic copper species at pH levels less than 6; the aqueous copper carbonate complex is dominant from pH 6.0 to 9.3 (USEPA 1980). This equilibrium is altered in the presence of humic acids, fulvic acids, amino acids, cyanide, certain polypeptides, and detergents (USEPA 1980). Most cupric salts dissolve readily in freshwater to produce the aquo ion, $Cu(H_2O)_6^{+2}$ (Leckie and Davis 1979). Divalent copper chloride, nitrate, and sulfate are highly soluble in water (USEPA 1980; Table 1), but copper carbonate, cupric hydroxide, cupric oxide, and cupric sulfide will precipitate from solution or form colloidal suspensions when excess cupric ions are present (USEPA 1980).

In seawater, the major chemical species of copper are Cu(OH)Cl and $Cu(OH)_2$ and these account for about 65% of the total copper in seawater (Boyle 1979). The levels of copper hydroxide ($Cu(OH)_2$) increase from about 18% of the total copper at pH 7.0 to 90% at pH 8.6; copper carbonate ($CuCO_3$) levels drop from 30% at pH 7.0 to less than 0.1% at pH 8.6 (USEPA 1980). The dominant copper species in seawater over the entire ambient pH range are copper hydroxide, copper carbonate, and cupric ion (USEPA 1980). Bioavailability and toxicity of copper in marine ecosystems is promoted by oxine and other lipid soluble synthetic organic chelators (Bryan and Langston 1992).

Copper concentrations in sediment interstitial pore waters correlate positively with concentrations of dissolved copper in the overlying water column and are now used to predict the toxicity of test sediments to freshwater amphipods (Ankley et al. 1993). Sediment-bound copper is available to deposit-feeding clams, especially from relatively uncontaminated anoxic sediments of low pH (Bryan and Langston 1992). The bioavailability of copper from marine sediments, as judged by increased copper in sediment interstitial waters, is altered by increased acid volatile sulfide (AVS) content (Casas and Crecelius 1994). But acid volatile sulfide is not an appropriate partitioning phase for predicting copper bioavailability of freshwater sediments (Ankley et al. 1993).

Metabolism

Copper is part of several essential enzymes including tyrosinase (melanin production), dopamine beta-hydroxylase (catecholamine production), copper-zinc superoxide dismutase (free radical detoxification), and cytochrome oxidase and ceruloplasmin (iron conversion) (Aaseth and Norseth 1986). All terrestrial animals contain copper as a constituent of cytochrome *c* oxidase, monophenol oxidase, plasma monoamine oxidase, and copper protein complexes (Schroeder et al. 1966). Excess copper causes a variety of toxic effects, including altered permeability of cellular membranes. The primary target for free cupric ions in the cellular membranes are thiol groups that reduce cupric (Cu^{+2}) to cuprous (Cu^{+1}) upon simultaneous oxidation to disulfides in the membrane. Cuprous ions are reoxidized to Cu^{+2} in the presence of molecular oxygen; molecular oxygen is thereby converted to the toxic superoxide radical (O^{-2}), which induces lipoperoxidation (Aaseth and Norseth 1986).

Aquatic Organisms. Bioavailability and toxicity of copper to aquatic organisms depends on the total

concentration of copper and its speciation (Hung et al. 1990). In hard, moderately polluted waters, 43 to 88% of the copper is associated with suspended solids and not available to biota (Shaw and Brown 1974). Copper toxicity to aquatic biota is related primarily to the dissolved cupric ion (Cu^{+2}) and possibly to some hydroxyl complexes (NAS 1977; Hall et al. 1988; Hung et al. 1990). Soluble copper is largely complexed with carbonate, amino acids, or humic substances. Cupric copper—one of the most toxic forms—constitutes 0.1 to 0.2% of this soluble material (Shaw and Brown 1974). The toxicity of copper in its complexed, precipitated, or adsorbed form is less than that of the free ionic form (Hall et al. 1988; Hung et al. 1990). In aquatic invertebrates, copper causes gill damage at high concentrations, and in fishes it interferes with osmoregulation (Hodson et al. 1979). Elevated concentrations of copper interfere with oxygen transport and energy metabolism; tissue hypoxia is the cause of death and is associated with reductions in the activities of regulatory enzymes of ATP-synthesizing pathways (Hansen et al. 1992b).

In freshwater algae, movement of copper into cells occurs mainly by physical transport; the plasmalemma is the initial site of copper binding. Copper on the plasmalemma increases its permeability, as shown by the leakage of potassium and other ions from copper-treated cells and entry of copper into intracellular sites (Stokes 1979).

Marine prosobranch gastropods, like several other groups of mollusks and arthropods, normally accumulate and store copper and use it in the synthesis of hemocyanin, a blood pigment (Betzer and Yevich 1975). In gastropods, copper may elicit secretions of mucus by goblet cells; bind to hydrophilic regions of the external membranes of epithelial cells, altering their biochemical and biophysical properties; or disrupt the normal functioning of peroxidase and ferritin (Cheng 1979). Peroxidation products, such as hydroperoxides and malondialdehyde, are toxic to vital functions of membranes and cells; bivalve mollusks challenged with ionic copper show significant increases in these products (Chelomin and Belcheva 1992). Exposure of gastropods to high sublethal concentrations of copper completely inhibits succinic dehydrogenase activity at whole body concentrations between 4.7 and 11.9 mg Cu/kg DW soft parts, causes a measurable decrease in heart beat rate, and adversely affects surface epithelia, especially those covering the head-foot and rectal ridge, disrupting osmoregulation and producing water accumulation in tissues (Cheng 1979). The primary lethal effect of copper in gastropod mollusks is caused by disruption of the transporting surface epithelium (Cheng 1979).

In crabs, the gills are a major target organ of copper toxicity; waterborne copper decreases hemocyanin-oxygen affinity (Truchot and Boitel 1992). Exposure of shore crabs (*Carcinus maenas*) to lethal concentrations of copper is associated with reductions in activity of glycolytic enzymes but, unlike fishes, did not involve cellular energy deprivation (Hansen et al. 1992b). Copper-tolerant strains of aquatic mayflies (*Baetis thermicus*) have evolved in Japan. Tolerance is attributed to the ability to induce a metal-binding protein that preferentially sequesters copper over cadmium and zinc (Suzuki et al. 1989).

In fishes, the gill surface's low affinity for metal allows greater entry of the metal to the intracellular compartment. Once there, more complex binding sites are present. Binding to these ligands causes one or more of the following toxic mechanisms: (1) blocking of the essential biological functional groups of biomolecules; (2) displacing the essential metal ion in molecules; or (3) modifying the active conformation of biomolecules. These mechanisms may account for the specific inhibition of ion transport from ionic copper (Cu^{+2}) exposure (Reid and McDonald 1991). Studies with radiocopper-64 and rainbow trout (*Oncorhynchus mykiss*) show that the external gill epithelial surface has a relatively low affinity for copper, allowing copper to penetrate intracellular compartments. Copper disrupts gill function of rainbow trout by impairing transepithelial ion exchange, for example, impairing or upsetting electrolyte balance by inhibiting active uptake or stimulating passive loss (Reid and McDonald 1991). Copper toxicity to rainbow trout in hard water is related to the total concentration of soluble copper (copper carbonate, $CuCO_3$; cupric ion, Cu^{+2}) in the test medium rather than to either of these two forms alone (Shaw and Brown 1974). Long-term retention of copper accumulations in fish tissues is characterized by high half-time persistence after copper administration and binding of copper to proteins in a nonexchangeable or slowly exchangeable pool (Carbonell and Tarazona 1994).

Copper detoxifying mechanisms in fishes include the induction of metallothioneins, allowing copper retention for weeks or months after absorption without producing toxic effects (Hogstrand et al. 1991; Hylland et al. 1992; Carbonell and Tarazona 1994; Marr et al. 1995). Hepatic metallothionein contents of individual fishes usually reflect the accumulation of copper in that organ (Hogstrand et al. 1991). This strongly supports the use of metallothionein as an indicator of copper stress (Hogstrand 1991).

In tench (*Tinca tinca*), hepatic alterations observed after exposure to lethal concentrations of copper (75 mg/L for 4 to 12 days) include accumulation of various pigments in Kupffer cells and hepatocytes. Death was attributed to deficient oxygen transport and consumption and to the lytic effect of copper on various cell membranes, eventually causing massive necrosis in large areas of the liver parenchyma (Roncero et al. 1992). In rapidly growing juvenile flounders (*Paralichthys* spp.), copper blocks calcium transport, possibly through interference with gill chloride cells. Copper inhibition of calcium accumulation is alleviated by removing copper from the medium (Dodoo et al. 1992).

Mammals. Copper homeostasis plays an important role in the prevention of copper toxicity. After copper requirements are met, excess copper absorbed into gastrointestinal mucosal cells is bound to metallothionein and excreted when the cell is sloughed. Copper that eludes the intestinal barrier is stored in the liver or incorporated into bile and excreted in feces. The most likely pathway for the entry of toxic amounts of copper would be long term inhalation or entry through the skin. Both of these pathways allow copper to pass unimpeded into the blood (ATSDR 1990). The levels of copper in the mammalian body are held constant by alterations in the rate and amount of copper absorbed, its distribution, and rate and route of excretion (ATSDR 1990). Many factors interfere with copper absorption including competition for binding sites, as with zinc; chelation, as with phytates; and interaction with ascorbic acid, which aggravates copper deficiency by decreasing copper absorption and—with excess copper—reduces the toxic effects (USEPA 1980; ATSDR 1990).

Two inherited human diseases that represent abnormal copper metabolism are Menkes' syndrome and Wilson's disease. Menkes' syndrome, with symptoms similar to those of copper deficiency, is characterized by a progressive brain disease, abnormally low copper concentrations in liver and other tissues, and diminished ability to transfer copper across the absorptive cells of the intestinal mucosa (USEPA 1980; Aaseth and Norseth 1986). Wilson's disease (hepatolenticular degeneration) is the only significant example of copper toxicity in humans. Wilson's disease is an autosomal recessive disorder that affects normal copper homeostasis and is characterized by excessive retention of hepatic copper, decreased concentration of serum ceruloplasmin, impaired biliary copper excretion, and hypercupremia. Systemic manifestations of Wilson's disease are hepatic and renal lesions and hemolytic anemia (Schroeder et al. 1966; Goresky et al. 1968; Baker 1969; USEPA 1980; Aaseth and Norseth 1986; ATSDR 1990). Certain strains of mutant rats with reduced excretion of biliary copper spontaneously develop hepatitis because of the extremely gross deposition of copper in the liver (Sugawara et al. 1994). Most humans afflicted with Wilson's disease usually die before puberty, although some survive to age 35 (Schroeder et al. 1966). Postmortems of Wilson's patients show that livers had as much as 7.5% copper and kidney ash had up to 2.7% copper. There is no evidence, however, that persons with normal homeostatic mechanisms are subject to any chronic degenerative disorders resulting from modern exposures to copper (Schroeder et al. 1966). Unusually susceptible human populations to copper poisoning include those afflicted with Wilson's disease, infants and children under age one year, those with liver damage or chronic renal disease, individuals undergoing dialysis (excess copper in the dialysate), and those with an inherited deficiency of the enzyme glucose-6-phosphate dehydrogenase (ATSDR 1990).

Ingested copper travels through the gastrointestinal (GI) tract, where some of it is absorbed into the blood and becomes associated with plasma albumin and amino acids (Sugawara et al. 1994) or is used to maintain copper levels in erythrocytes (USEPA 1980). Albumin-bound copper is eventually transported to the liver; however, minor fractions are transported into the bone marrow, the erythrocytes, or other tissues (Aaseth and Norseth 1986). Most of the circulating copper is translocated within minutes. During the next few hours, blood copper concentrations increase and copper becomes an integral part of the ceruloplasmin molecule (Goresky et al. 1968). Gastrointestinal absorption is normally regulated by the copper status in the body. In general, up to 50% of small doses (i.e., less than 1 μg in rats) are absorbed, whereas large doses are absorbed to a lesser extent (Aaseth and Norseth 1986). In humans, about 40% of the dietary copper is absorbed (USEPA 1980). Absorbed copper is freely exchangeable with copper loosely bound to the alpha-globulin ceruloplasmin where it is exchanged in the cupric form (Schroeder et al. 1966). Copper is stored mainly in liver, brain, heart, kidney, and muscle; in tissues and blood cells, copper is bound to proteins, including many enzymes (Aaseth and Norseth 1986). Amino acids facilitate the entry of copper into liver cells and a small proportion of copper in serum is bound to amino acids (Goresky et al. 1968). About 80% of the absorbed copper is bound to metallothionein in the liver; the remainder is incorporated into compounds such as cytochrome *c* oxidase (USEPA 1980; ATSDR 1990). Copper accumulations in animals are associated with increased number and increased size of copper-containing lysosomes in hepatocytes. In liver, copper is initially bound to a metallothionein-like, low molecular-weight protein and later it appears in a high-molecular weight protein, ceruloplasmin, which reenters the circulation. Ceruloplasmin transports copper to tissues and also functions as an oxidase (Aaseth and Norseth 1986). The amount of copper absorbed is usually far in excess of metabolic requirements (Sugawara et al. 1994). Of the copper retained in the body, almost all plays a particular physiological role in the function of at least 12 specific copper proteins, such as cytochrome *c* oxidase and tyrosinase. Thus, only extremely small concentrations of free copper ions are normally found in body fluids (NAS 1977).

Retention of radiocopper injected into humans is high; only 10% is excreted within 72 h in urine and feces and 50% in four weeks (Aaseth and Norseth 1986). Most (72%) of the unabsorbed copper is excreted in the feces primarily by way of the biliary duct, the salivary glands, or the intestinal mucosa; a minor portion is excreted by way of sweat and menses (Schroeder et al. 1966; USEPA 1980; ATSDR 1990). In mammals, copper is excreted mainly via the bile in association with glutathione or unidentified high molecular weight molecules; however, the transport mechanisms of copper from liver cells into bile are essentially unknown

(Aaseth and Norseth 1986). In rats, biliary excretion of copper is increased by increased flow of bile, increased body temperature, or administration of adrenal steroids (Sugawara et al. 1994).

Mechanisms implicated in copper poisoning include free radical production, alteration in activities of several enzymes, and interference with metallothionein synthesis. At the cellular level, copper has several primary mechanisms of toxicity that alter protein configuration and biological activity. These include the catalysis of peroxidation reactions and subsequent generation of free radicals that damage lipids and proteins, interactions with R groups of proteins—particularly SH groups, and acting as a substituent for other metals in metalloproteins (Sanders et al. 1994). Copper, in relative excess, is a cytotoxic metal with injury related to the process of lipid peroxidation. Isolated rat hepatocytes exposed to copper solutions for as long as 90 min show a concentration- and time-related decrease in cell viability as judged by loss of intracellular potassium and aspartate aminotransferase, an increase in lipid peroxidation, and a decrease in glutathione (Stacey and Klaassen 1981). Falling disease in cattle, dogs, and chickens is associated with a cardiovascular disorder caused by reduced activity of lysal oxidase, a copper-requiring enzyme necessary for elastic tissue formation and maintenance (USEPA 1980). Metallothionein synthesis acts as a protective mechanism against buildup of excessive amounts of the essential, but potentially toxic, copper ions, possibly before the development of other control processes. In livers of newborn lambs, rabbits, mice, and hamsters copper concentrations are usually directly related to the metallothionein content in cytoplasmic fractions (Bakka and Webb 1981). In sheep, elevated serum glutamic oxaloacetic transaminase (SGOT) levels were linked to elevated copper concentrations in blood at least one to six weeks before obvious external signs of copper poisoning. SGOT measurements in sheep serum seem to constitute an adequate early warning of the approach of the hemolytic crisis and eventual death of the animal from chronic copper poisoning (MacPherson and Hemingway 1969).

Interactions

Copper interacts with numerous compounds normally found in natural waters. The amounts of the various copper compounds and complexes present in solution depend on water pH, temperature, and alkalinity and on the concentrations of bicarbonate, sulfide, and organic ligands (USEPA 1980). In animals, copper interacts with essential trace elements such as iron, zinc, molybdenum, manganese, nickel, and selenium and also with nonessential elements including silver, cadmium, mercury, and lead; interactions may be either beneficial or harmful to the organism (Kirchgessner et al. 1979). The patterns of copper accumulation, metabolism, and toxicity from these interactions frequently differ from those produced by copper alone. Acknowledgment of these interactions is essential to understanding copper toxicokinetics.

Aluminum

Mixtures of copper and aluminum (Al) were more than additive in toxicity to ova of brown trout, *Salmo trutta* (Sayer et al. 1991).

Cadmium

Exposure of algae to low sublethal concentrations of copper (0.03 µg/L) increases their sensitivity towards additional copper challenge and to cadmium (Cd) salts (Visviki and Rachlin 1994a). In freshwater clams (*Anodonta cygnea*) exposed for 46 days to a mixture of high concentrations of copper (139 µg/L) and cadmium (122 µg/L), cadmium accumulation is reduced 90% and copper accumulation reduced 50% (Holwerda 1991). Exposure of crayfish (*Cambarus bartoni*) to 12.5 µg Cd/L for 72 h results in significantly increased copper stores in the hepatopancreas; however, isopods similarly exposed had decreased copper stores in antennal glands (Mwangi and Alikhan 1993). In the presence of copper, barnacles tend to accumulate cadmium (Powell and White 1990). In fishes, copper-cadmium interactions occur in Mozambique tilapia (*Oreochromis mossambicus*) during single and combined exposures. Waterborne copper tends to increase whole body cadmium content of tilapia at all tested copper concentrations and exposure durations (as high as 400 µg Cu/L for 96 h); however, cadmium exposure tends to lower copper concentrations in tissues of tilapia (Pelgrom et al. 1994).

In birds, copper concentrations in kidneys of the willow ptarmigan (*Lagopus lagopus*) are positively correlated with concentrations of cadmium (Wren et al. 1994).

In mammals, cadmium inhibits copper absorption across the intestinal mucosa (Aaseth and Norseth 1986). Intercorrelations of copper with cadmium and zinc in livers of polar bears (*Ursus maritimus*) are probably mediated by metallothioneins, which may contain all three metals (Braune et al. 1991). In rats, copper protects against nephrotoxicity induced by cadmium, provided that copper is administered 24 h prior to cadmium insult. Specifically, rats given 12.5 mg Cu/kg BW by way of subcutaneous injection 24 h before receiving 0.4 mg Cd/kg BW—when compared to a group receiving Cd alone—did not have excessive calcium in urine and renal cortex or excessive protein in urine; thus, 2.8 mg Cu/kg BW protects against 0.25 mg Cd/kg BW (Liu et al. 1992).

Iron

Mixtures of copper and iron (Fe) salts were more than additive in toxicity to ova of brown trout (Sayer et al. 1991).

In muscle of Weddell seals (*Leptonychotes weddelli*), copper is positively correlated with iron (Szefer et al. 1994). In general, concentrations of copper in all tissues of all marine vertebrates examined are positively correlated with concentrations of iron (Eisler 1984).

The primary function of the mammalian red blood cell is to maintain aerobic metabolism while the iron atom of the heme molecule is in the ferrous (Fe^{+2}) oxidation state; however, copper is necessary for this process to occur (USEPA 1980). Excess copper within the cell oxidizes the ferrous iron to the ferric (Fe^{+3}) state. This molecule, known as methemoglobin, is unable to bind oxygen or carbon dioxide and is not dissociable (Langlois and Calabrese 1992). Simultaneous exposure of sheep to mixtures of cupric acetate, sodium chlorite, and sodium nitrite produced a dose-dependent increase in methemoglobin formation (Calabrese et al. 1992; Langlois and Calabrese 1992).

The addition of iron to diets of domestic pigs increases their resistance to copper poisoning (USEPA 1980), but this is an exception. High intake of iron, in general, adversely affects copper status in ruminants, guinea pigs, and rats; the mechanisms for this phenomenon are unknown (Yu et al. 1994). Genetically anemic and normal strains of rats fed high iron diets had reduced kidney copper concentrations in both groups; this was associated with decreased absorption and biliary excretion of copper (Yu et al. 1995).

Manganese

Copper in livers and muscles of Weddell seals was positively correlated with manganese (Mn; Szefer et al. 1994). In general, manganese and copper are positively correlated in tissues of marine vertebrates (Eisler 1984). Uptake of copper from copper-contaminated freshwater sediments by annelid worms is related to the amount of reducible manganese oxide in the sediments (Diks and Allen 1983).

Molybdenum

In terrestrial vegetation, molybdenum (Mo) and sulfur interfere with copper-induced deficiencies (Gupta 1979). Copper poisoning in cattle and other ruminants is governed by dietary concentrations of molybdenum and sulfate (Lewis et al. 1967; Todd 1969; Buckley and Tait 1981; Eisler 1989). Molybdenum and sulfur in mammalian diets cause a decrease in the availability of copper because of the formation of the biologically unavailable copper-thiomolybdate complex (Aaseth and Norseth 1986). Cattle die when grazing for extended periods on pastures where the ratio of copper to molybdenum is less than 3 to 1, or if they are fed low copper diets containing molybdenum at 2 to 20 mg Mo/kg ration (Eisler 1989). Wilson's disease is induced in rabbits by feeding a diet high in molybdates and sulfates, suggesting that the disease is not solely the result of copper intoxication (Goresky et al. 1968).

Zinc

Copper is positively correlated with zinc in gills of two species of fishes from the Mediterranean Sea (Romeo et al. 1994). Mixtures of copper and zinc salts in marine or freshwater fishes are more-than-additive in toxicity, producing more deaths in 96 h than expected on the basis of individual components (Eisler and Gardner 1973; Birge and Black 1979; Hodson et al. 1979). Mixtures of copper and zinc are generally acknowledged to be more-than-additive in toxicity to a wide variety of aquatic organisms (Birge and Black 1979; Hodson et al. 1979; Fernandez and Jones 1990; Eisler 1993). But mixtures of copper (0 to 90 µg/L) and zinc (0 to 1,200 µg/L) are only additive in action to a marine bacterium (*Photobacterium phosphoreum*), decreasing its luminescence after exposure for 30 min (Parrott and Sprague 1993). And sometimes mixtures of copper and zinc salts are less-than-additive in action, as judged by DNA, RNA, and protein contents of newly hatched fathead minnows (*Pimephales promelas*) exposed for 4 days (Parrott and Sprague 1993).

In birds, copper and zinc are positively correlated in kidneys of the willow ptarmigan (*Lagopus lagopus*; Wren et al. 1994) and in kidneys and livers of common murres (*Uria aalge*; Stewart et al. 1994).

In mammals, copper absorption across the intestinal mucosa is inhibited by concomitant high oral intake of zinc (Aaseth and Norseth 1986). In livers from Weddell seals, copper is positively correlated with zinc (Szefer et al. 1994). The addition of zinc to swine diets protects against copper toxicosis caused by eating diets containing 250 mg Cu/kg ration (USEPA 1980).

Other Inorganics

Copper interacts with lead (Pb), magnesium (Mg), silver (Ag), and other elements. In mammals, supplemental copper promotes urinary excretion of lead from the body and loss of lead from tissues (Flora 1991). In shore crabs (*Carcinus maenas*), ionic copper displaces ionic magnesium in gills, leading to inhibition of phosphoryl transfer (Hansen et al. 1992b). In embryos of the Pacific oyster (*Crassostrea gigas*), silver—at 0.5 to 15.5 µg Ag/L—enhances adverse effects when copper concentrations exceed 6.0 µg Cu/L (Coglianse and Martin 1981). Silver positively correlates with copper in livers of Weddell seals, but in muscles the correlation is negative (Szefer et al. 1994).

In fishes, additive or more-than-additive toxicity occurs with mixtures of salts of copper and mercury, copper-zinc-phenol, and copper-nickel-zinc (Birge and Black 1979). Accumulation of copper in gills of fathead minnows during exposure to 16 µg Cu/L is reduced by added ionic calcium, which competes with copper for gill binding sites (Playle et al. 1992).

Organic Compounds

Sequestering agents, increasing salinity, sediments, and other variables all reduce toxicity and accumulation of copper in tested species of aquatic plants and invertebrates. Chelating agents, such as nitrilotriacetic acid, reduce the toxicity of ionic copper to six species of estuarine phytoplankton (Erickson et al. 1970). Sensitivity of freshwater zooplankton communities varies seasonally. Communities are most sensitive to copper stress (20 or 40 µg Cu/L)

during exposure for 5 weeks in spring rather than in summer or autumn because, in part, of reduced dissolved organic carbon concentrations in the spring (Winner et al. 1990). Adverse effects of copper on survival of marine copepods are reduced or eliminated by the presence of clay minerals, diatoms, ascorbic acid, sewage effluents, water extracts of humic acids, and certain soil types (Lewis et al. 1972). Chelators, such as EDTA, and more alkaline pH increase the survival and larval developmental rates of copepods challenged with copper through increased complexation of cupric ions (Sunda et al. 1990). Natural fulvic acids, which comprise 75% of dissolved humic substances, reduce the acute toxicity of copper to rotifers (Porta and Ronco 1993). A significant reduction in radiocopper-64 accumulation by clams (*Macoma balthica*) occurs at high concentrations of dissolved organic ligands; reduction is more pronounced at 3.0% salinity than 1.0% salinity (Absil et al. 1993). The presence of sediments in assay containers reduces the toxicity of copper to freshwater gastropods (Winger et al. 1984). Copper uptake by brine shrimp (*Artemia franciscana*) increases with decreasing pH and decreasing carbonate complexation (Blust et al. 1991). Studies with a freshwater shrimp (*Paratya australiensis*) and copper salts show that uncomplexed cupric ions are the most toxic chemical species in solutions containing nitrilotriacetic acid or glycine; however, the singly charged copper-glycine^{+} complex also appears to be mildly toxic (Daly et al. 1990a). Shrimp (*Paratya* sp.) are more resistant to copper in higher alkalinity waters (Daly et al. 1990b) and under conditions of increasing dissolved organic matter (Daly et al. 1990c).

In freshwater fishes, mixtures of copper with anionic detergents or various organophosphorus insecticides cause more-than-additive toxicity (Hodson et al. 1979). And in marine vertebrates, copper in tissues is positively correlated with metal-binding proteins (Eisler 1984). Accumulations of copper in gills of fathead minnows during exposure to 16 µg Cu/L is reduced by added EDTA, which reduces bioavailability of copper through complexation (Playle et al. 1992). Copper LC50 (96 h) values (i.e., concentrations of ionic copper in solution at the start of the test estimated to kill 50% of the test species in 96 h) to larval fathead minnows range from a low of 2 µg/L at low pH and low dissolved organic carbon to 182 µg/L at pH 6.9 and dissolved organic carbon of 15.6 mg/L (Welsh et al. 1993). Acidification and the removal of dissolved organic carbon increases the toxicity of copper to fathead minnows in natural waters of low alkalinity and explains 93% of the variability in field toxicity data for that species (Welsh et al. 1993).

In mammals, phenobarbital and phenytoin increase serum ceruloplasmin concentrations (Aaseth and Norseth 1986). Chronic copper poisoning in sheep is exacerbated when diets contain heliotrope plants (*Heliotropium* sp., *Echium* spp., *Senecio* sp.). Aggravated effects of the heliotrope plants include reduced survival and a twofold to threefold increase in liver and kidney copper concentrations when compared to control animals fed copper without heliotropes (Howell et al. 1991). Rats given acutely toxic doses of 2,3,7,8-tetrachlorodibenzo-para-dioxin had elevated concentrations of copper in liver and kidney because of impaired biliary excretion of copper (Elsenhans et al. 1991). Morphine increases copper concentrations in the central nervous system of rats, and dithiocarbamates inhibit biliary excretion (Aaseth and Norseth 1986). In human patients, urinary excretion of copper is increased after treatment with D-penicillamine, calcium disodium EDTA, or calcium trisodium diethylenetriamine penta acetic acid (Flora 1991).

Carcinogenicity, Mutagenicity, Teratogenicity

General

No definitive evidence exists demonstrating that copper or copper compounds at environmentally realistic concentrations are the causative agents in the development of carcinogenicity, mutagenicity, or teratogenicity (USEPA 1980; Aaseth and Norseth 1986; ATSDR 1990). However, under controlled conditions of grossly elevated exposures, some studies suggest that copper is a potential carcinogen in rodents (USEPA 1980; ATSDR 1990; Toussaint and Nederbragt 1993); mutagen in rodents (Aaseth and Norseth 1986; ATSDR 1990), sheep (Bires et al. 1993), and grasshoppers (Bhunya and Behura 1986); and teratogen in fish (Birge and Black 1979), rodents, and other small laboratory animals (Aaseth and Norseth 1986).

Carcinogenicity

The carcinogenic classification of copper is Group 3 or D; that is, not classifiable as to its carcinogenicity in humans (ATSDR 1990). No definitive evidence exists showing that copper or copper compounds cause cancer in mammals (USEPA 1980; Aaseth and Norseth 1986; ATSDR 1990). Although hypercupremia is sometimes associated with neoplasms (USEPA 1980), some copper compounds seem to have an inhibitory effect on the development and growth of malignant tumor cells (Aaseth and Norseth 1986). Copper is not associated with an elevated incidence of cancer in humans or animals exposed by way of inhalation, oral, dermal, or intramuscular injection routes. A slightly increased incidence of reticulum cell sarcoma was noted in mice 18 months after a single subcutaneous injection of copper 8-hydroxyquinoline, but this needs to be verified (ATSDR 1990).

Sensitivity of cancerous cells to copper may reflect cell DNA content. Two closely related rat hepatoma cell lines differed in sensitivity to copper toxicity by a factor of four; DNA content in each cell line decreased with increasing copper concentrations, but at different rates. Severity of toxicity was associated with increasing accumulations of

copper in the cell nucleus and with decreasing DNA (Toussaint and Nederbragt 1993).

Mutagenicity

Grasshoppers (*Oxya velox*) injected intra-abdominally with relatively high concentrations of soluble copper showed a 1.6% frequency of chromosomal anomalies in meiotic cells of testes 24 h after injection (Bhunya and Behura 1986); however, no control data were presented. Copper-induced DNA strand breaks in rats and chromosomal aberrations and sperm abnormalities in mice suggest that copper is a potential human mutagen (ATSDR 1990). Copper salts affect chromosomes in vitro in the presence of hydrogen peroxide and ascorbic acid and can also increase the frequency of non-complementary nucleotides in the synthesized DNA double helix (Aaseth and Norseth 1986). Sheep, age 1.5 years, given about 10.7 mg Cu/kg BW daily—in addition to other metals—until they died (65 to 84 days later) show a significant increase in sister chromatid exchanges in bone marrow (Bires et al. 1993); however, the specific role of copper on survival and mutagenicity is unclear and requires verification.

Teratogenicity

Grossly elevated concentrations of dissolved copper produce teratogenicity in fish embryos. A significant number of malformed fish larvae came from eggs treated with 500 µg Cu/L (Birge and Black 1979). In studies with laboratory animals and elevated concentrations of copper salts, copper penetrates the placental barrier into the fetus; intramuscular injection of 4 mg Cu/kg BW early in pregnancy adversely affects fetal central nervous system development (Aaseth and Norseth 1986). In humans, no definitive data are available on whether copper can cause birth defects; however, incubation of human spermatozoa with metallic copper results in loss of sperm motility (Aaseth and Norseth 1986).

Concentrations in Field Collections

General

Copper concentrations in air, soil, water, sediments, and other abiotic materials are elevated as a result of human activities, especially near copper smelters and mines, urban areas, municipal and industrial wastewater outfalls, marinas containing copper-based antifouling paints, and agricultural soils receiving prolonged applications of copper-based fungicides (Table 2). Maximum copper concentrations in selected abiotic materials are 5 µg/m³ in air, 5 µg/L in groundwater, 12 µg/L in rainwater, 300 mg/kg DW in black shales, 1,200 mg/kg DW in poultry litter, 6,500 mg/kg DW in marine sediments, 7,000 mg/kg DW in soils, and 7,700 mg/kg DW in sewage sludge (Table 2).

Table 2. Copper concentrations in selected abiotic materials.

Material, units of concentration, and other variables	Concentration[a]	Reference[b]
Air, µg/m³		
Near copper smelters	1-2; Max. 5.0	1, 2
Nonurban locations	0.16-0.21; Max. 1.2	3
Remote locations	Usually <0.001; sometimes 0.001-0.003; Max. 0.012	4
South Pole	0.00004	5
Urban locations	0.15-0.18; Max. 1.6	4
United States	0.01-0.67	5
U.S. cities	Usually 0.09-0.81; sometimes 0.81-2.4; infrequently >2.4	2, 6
Uncontaminated	0.001-0.2	1, 7
Coal, µg/kg dry weight (DW)	17,000	7
Drinking water, µg/L		
Conducted via copper pipes	Max. 1,000	1
Private houses		
White Plains, New York	540	6
Bridgeport, Connecticut	185	6
Vermont		
Private houses	75-1,400	6
Hospital	17-730	6
United States	134; Max. 8,350	1, 2
Glaciers, µg/kg fresh weight (FW)	0.2	7
Groundwater, µg/L		
New Jersey	About 5.0	1

Table 2. *Continued.*

Material, units of concentration, and other variables	Concentration[a]	Reference[b]
Lakes and rivers, µg/L		
Canada	1-8	1
Contaminated vs. noncontaminated	50-100 vs. 1-7	6
Lake Asosca, Nicaragua, 1991-92	Usually <2.0; mean 3.1; Max. 13.1	8
Ligurian Sea drainage	<0.3-1.75 (equivalent to 3.5-7.1 tons annually)	22
New Jersey	3.0	1
Sweden; near brassworks vs. reference site	9.4 vs. 1.0	21
United States	5.3 (0.83-105.0); usually <2.0-4.2	1, 5, 7
Manure, µg/kg DW		
Cattle	5,000	1
Mine tailings, mg/kg DW		
Butte Lake, Canada, 1982	7,100	9
Municipal water supplies, µg/L	8.3 (0.6-250.0)	6
Oil, µg/kg FW		
Crude	140	7
Shale	70,000	7
Pond water, µg/L		
Massachusetts	(<10-105)	1
Poultry litter, mg/kg DW	1,196	10
Precipitation, µg/L		
Soluble vs. total	6.0 vs. 12.3	4
Rocks, µg/kg DW		
Crustal and sedimentary	24,000-45,000	6, 7
Sandstones	10,000-40,000	11
Shales	30,000-150,000	11
Marine black shales	20,000-300,000	11
Seawater, µg/L		
Central Texas coast	Max. 50.0	12
Chesapeake Bay, Maryland; 1985-86; dissolved	11.7 (ND-80.0)	13
In water flowing through copper pipes	45.0	6
Mediterranean, northwestern coast	Max. 22.4	12
North Sea	0.2-2.6	14
Oceanic		
Dissolved	0.15	7
Total	0.06-6.7	5, 12, 13
Surface waters		
Atlantic Ocean	0.06-0.21	1
East Arctic Ocean	0.13	1
Taiwan, coastal		
Total	10.2	15
Particulate	2.49	15
Dissolved	7.75	15
Labile	2.19	15
Inorganic labile	2.15	15
Free labile	0.04	15
Nonlabile	5.56	15
Polar nonlabile	3.81	15
Nonpolar nonlabile	1.75	15
Taiwan, near copper recycling facility		
Total	0.8-737.0	15
Dissolved	3.5-36.5	15
Particulates	0.2-723.0	15

Table 2. *Continued.*

Material, units of concentration, and other variables	Concentration[a]	Reference[b]
United Kingdom estuaries		
Contaminated	3-176	14
Noncontaminated	2-3	14
Sediments, mg/kg DW		
England and Wales, streams	7-70	17
Lake Asosca, Nicaragua; 1991-92	(36.6-73.7)	8
Long Island Sound, New York; 1984-85	190	18
Southwest England		
Carnon River (water 1,080 µg/L)	1,650: Max. 6,500	14
Fowey (water 7-21 µg/L)	50; Max. 370	14
Red River (water 17-35 µg/L)	590	14
Sweden; freshwater lakes; 1988		
3-5 km from smelter	707-2,531	19
50-80 km from smelter	37-54	19
United Kingdom estuaries, contaminated vs. noncontaminated	>2,000 vs. 10	14
Sediment interstitial waters, µg/L		
Butte Lake, Canada; 1982	Max. 14.8	9
Clean vs. copper-contaminated sediments	<10 vs. 100	14
Sewage sludge, mg/kg DW		
Missouri	390 (45-5,200)	16
Primary sludge	21 (3-77)	1
United States, 23 cities	991 (126-7,729)	1
Soils, mg/kg DW		
Global	(2-250)	1, 5
Italy	51	20
Near copper production facility	7,000	1
To 100 cm depth		
Total	20	7
Organic fraction	350	7
Under oak trees	3.5	6
Under maple trees	6.0	6
United States	19 (1-70)	11, 16

[a]Concentrations are shown as means, range (in parentheses), maximum (Max.), or nondetectable (ND).
[b]1, ATSDR 1990; 2, USEPA 1980; 3, Nriagu 1979a; 4, Nriagu 1979d; 5, Aaseth and Norseth 1986; 6, Schroeder et al. 1966; 7, Nriagu 1979c; 8, Cruz et al. 1994; 9, Pedersen 1983; 10, van der Watt et al. 1994; 11, NAS 1977; 12, Neff and Anderson 1977; 13, Hall et al. 1988; 14, Bryan and Langston 1992; 15, Hung et al. 1990; 16, Beyer 1990; 17, Thornton 1979; 18, Turgeon and O'Connor 1991; 19, Johnson et al. 1992; 20, Arduini et al. 1995; 21, Hogstrand et al. 1991; 22, Migon 1993.

Copper concentrations in field collections of plants and animals are usually elevated in areas treated with copper-containing herbicides, near smelters, and from heavily urbanized and industrialized areas (Stokes 1979; Eisler 1984; Winger et al. 1984; Read and Martin 1993; Swiergosz et al. 1993; Fishelson et al. 1994; Storm et al. 1994). The amount and distribution of copper in animal tissues varies with tissue, organism age, sex, and amount of copper in the diet (Cuill et al. 1970; NAS 1977; USEPA 1980; Fishelson et al. 1994). Additional and more detailed information on copper concentrations in field collections of plants and animals is found in Jenkins (1980) and Eisler (1979, 1981).

In terrestrial vegetation, copper is usually less than 35 mg/kg DW except near smelters, where it may approach 700 mg/kg DW, and in copper-accumulator plants that may normally contain as much as 13,700 mg/kg DW (Table 3).

Table 3. Copper concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in field collections of representative plants and animals.

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Terrestrial Plants		
Red maple, *Acer rubrum*; leaf; Ontario, Canada; distance from smelter		
1.6 km	37 DW	1
2.6 km	26 DW	1
10.4 km	19 DW	1
28.9 km	16 DW	1
Copper plant mint, *Aeolanthus biformifolius*; Zaire		
Leaf	2,150-2,600 DW	1
Flower stem	2,150-3,500 DW	1
Corm	2,600-13,700 DW	1
Whole	10,000-13,700 DW	1
Agricultural crops, various	3-36 DW	2
Hair grass, *Deschampia flexuosa*; Ontario, Canada; distance from smelter		
1.7 km	726 DW	1
2.1 km	121 DW	1
7.4 km	103 DW	1
52.7 km	13 DW	1
Ferns, seven species; leaves	0.51 (0.22-0.98) FW	1
Fungi		
Seven species, whole	2.4 (1.5-3.0) FW	3
Various species		
Cap	Max. 131.7 DW	1
Spore	Max. 165.0 DW	1
Stalk	Max. 14.2 DW	1
Whole	Max. 95.9 DW	1
Grasses, various species	5 DW	2
Moss, *Hypnum cupressiforme*		
Wales; distance downwind from smelter		
Up to 3 km	All dead	1
8 km	62-68 DW	1
25 km	18-19 DW	1
Control site	11 DW	1
Sweden; near industries	Max. 265-580 DW	1
Legumes, various	15 DW	2
Lichens, various species		
Arctic	5 DW	4
Near copper smelter; Sudbury, Ontario	(15-20) DW	4
Tomato, *Lycopersicon esculentum*; United States		
Fruit	14 (8-34) DW	1
Leaf	(3-12) DW	1
Terrestrial plants, various species; seeds	1.1 (0.6-2.9) FW	3
Poppy, *Papaver orientale*; pods	14.3 FW	3
Lichen, *Parimelia baltimorensis*; Washington, D.C.; various years		

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
1938	17 DW	1
1958	22 DW	1
1970	32 DW	1
Norway spruce, *Picea abies*		
Connecticut		
Leaf	6.0 DW	1
Twig	15.0 DW	1
England		
Bark	5.0 DW	1
Wood	0.6 DW	1
Sweden		
Bark	25.0 DW	1
Needle	(4.4-8.1) DW	1
Root	(8-21) DW	1
Twig	(42-76) DW	1
Wood	2.0 DW	1
Trees, various species; leaves	1.8 (0.6-5.2) FW	3
Tundra plants; whole; Spitsbergen, Norway; 1987		
Lichens, 14 species	1.8-36.7 DW	5
Mosses, four species	3.4-33.0 DW	5
Vascular plants, five species	3.9-10.0 DW	5
Elm, *Ulmus americana*; wood	7.9 FW	3
Corn *Zea mays*		
Grain		
East Asia	1.6 FW	1
Lower Dahomey	(1.0-2.9) DW	1
United States	8 (4-17) DW	1
From soils with Cu additions of 360 kg Cu/ha		
Grain	1.7-2.8 DW	6
Leaves	7.8-12.5 DW	6
Aquatic plants		
Algae and macrophytes; 11 species; Brazil; November 1989; whole	2.4-6.9 DW	14
Alga, *Ascophyllum nodosum*		
England; polluted bay vs. reference site	68 (46-96) DW vs. 12 (6-18) DW	1
Norway; polluted fjord vs. reference site	(45-240) DW vs. 5.5 (4-8) DW	1
Freshwater macrophytes; various species	2.5-256.0 DW	15
Water milfoil, *Myriophyllum* spp.	10.0-41.3 DW	1
Brown alga, *Pelvetia canaliculata*; whole		
Norway	55 DW	1
Scotland	5-16 DW	1
Pondweed, *Potamogeton* spp.; whole; Pennsylvania	5.0-102.9 DW	1
Eelgrass, *Zostera* spp.		
Denmark; 1979-80; metals-contaminated site vs. reference site		
Leaves	9-13 DW vs. 5-6 DW	16
Roots	27.4 DW vs. 6-7 DW	1

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Portugal and Spain; contaminated bay vs. reference site	1,350 DW vs. (9-36) DW	1
Porifera		
Sponges; three species; whole	13-34 DW	1
Coelenterates		
Jellyfish, *Cyanea capillata*; whole		
New England	8.2 DW	1
Sweden	68.0 DW	1
Octacorals; Venezuela; whole; five species	0.9-3.1 DW	17
Terrestrial invertebrates		
Honeybee, *Apis mellifera*; Czechoslovakia; industrial locations vs. reference site; 1986-87		
Foraging workers	32-37 DW vs. 20-24 DW	7
Honey	1.1-1.7 DW vs. 0.6 DW	7
Pollen	6.1-8.2 DW vs. 5.4 DW	7
Landsnail, *Arianta arbustorum*; urban areas vs. reference site; Innsbruck, Austria; 1987; soft parts	188 (30-408) DW vs. 84 (46-104) DW	8
Bumblebee; four species of *Bombus*; queens; whole; Sweden, April 1991	18-23 (11-38) DW	9
Pine moth, *Bupalus piniarius*; pupae; whole; Finland, 1987; industrialized area vs. reference site	Max. 137 DW vs. 53 DW	10
Earthworm, *Lumbricus rubellus*; Cardiff, Wales; 1984; contaminated soils (2,740 mg Cu/kg DW soil) vs. reference site (26 mg Cu/kg DW soil)		
Anterior alimentary canal	85.4 DW vs. 18.2 DW	11
Posterior alimentary canal	64.4 DW vs. 21.1 DW	11
Remainder	23.2 DW vs. 10.1 DW	11
17-year cicadas, *Magicicada* spp.; Maryland; 1987; whole	(33.2-60.3) DW	12
Pine noctuid, *Panolis flammea*; pupae; whole; Finland, 1987; industrialized area vs. reference site	Max. 89 DW vs. 20 DW	10
Cuckoo bumblebee, *Psithyrus bohemicus*; queens; Sweden; April, 1991; whole	19 (12-29) DW	9
Spiders, whole; from old-field subjected to 11 years of nutrient enrichment (3,410 g Cu/ha yearly) vs. reference site (2-3 g Cu/ha yearly)		
Garden orb weaver, *Argiope aurantia*	110 DW vs. 80 DW	13
Wolf spiders, Lycosidae	130 DW vs. 85 DW	13
Aquatic mollusks		
Antarctic scallop, *Adamussium colbecki*; Ross Sea; 1987-88 vs. 1990		
Digestive gland	12.6 vs. 3.5 FW	18, 19
Gills	6.5 DW vs. 1.4 FW	18, 19
Gonad	4.7 DW vs. ND	18
Kidney	4.0 DW vs. ND	18
Mantle	3.5 DW vs. ND	18
Muscle	1.6 DW vs. ND	18

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Freshwater mussel, *Amblema* sp.; Texas		
Digestive gland	9.5 FW	1
Foot	2.9 DW	1
Gill	6.1 DW	1
Mantle	3.6 DW	1
Blood clam, *Anadara granosa*; soft parts; Malaysia	0.7-0.8 FW; 6.3 (4.5-8.0) DW	20, 21
Freshwater mussel, *Anodonta grandis*; soft parts; Manitoba, Canada; 1986	45.3 (5-80) DW	22
Lake mussel, *Anodonta piscinalis*; gills		
No glochidia	5.4 DW	23
With glochidia	8.0 DW	23
Ocean quahog, *Arctica islandica*		
Soft parts		
Block Island Sound	10.0 DW	24
Chesapeake Bay	5.4 DW	24
Georges Bank	3.5-10.3 DW	24
New York Bight	11.3 DW	24
Western Baltic Sea, 1992-93		
Adductor muscle	1.8-2.2 DW	24
Digestive gland	13.5 DW	24
Foot	3.1 DW	24
Gills	6.7 DW	24
Kidney	40.1 DW	24
Mantle	5.0 DW	24
Soft parts	14.3-15.3 DW	24
Whelk, *Buccinum undatum*; soft parts		
Irish Sea	180 DW	1
Scotland	78 DW	1
Channeled whelk, *Busycon canaliculatum*		
Digestive gland	(32-1,135) FW	1
Muscle	(12-21) FW	1
Cephalopods; liver	150 FW	3
Scallop, *Chlamys operculis*		
Kidney	240.0 FW	1
Shell	2.1 FW	1
Soft parts	1.7 FW	1
Pacific oyster, *Crassostrea gigas*		
Shell	(1.6-2.9) DW	1
Hong Kong, 1989; various locations		
Gill	840 DW	25
Mantle	509 DW	25
Muscle	750 DW	25
Soft parts	344-422 DW; max. 1,071 DW	25
Visceral mass	383 DW	25
Arcachon Bay, France, soft parts		
1979-82	48.3-63.8 DW	26
1983-87	67.7-116.2 DW	26

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
1988-91	101.8-135.0 DW	26
Soft parts		
England	(340-6,480) DW	1
South Africa	33.0 DW	1
Tasmania	(9.4-84.4) DW	1
United States	(7.8-38.0) FW	1
Taiwan		
Soft parts; 1989; seawater had 5.0-23.6 µg Cu/L from discharges of copper recycling facility	4,401 DW; green in color	27
Soft parts		
From copper-contaminated environment	2,225 DW	28
As above; after 6 days in clean seawater	746 DW	28
As above; after 32 days in clean seawater	344 DW	28
American oyster, *Crassostrea virginica*		
Florida, soft parts		
From a canal lined with chromated-copper-arsenate wood vs. reference site	150-200 FW vs. 10 FW; elevated concentrations were associated with greenish color and higher frequency of histopathology of digestive gland diverticula	29
Reference site oysters transplanted into above canal		
After 3 months	130 FW	29
After 4 months	220 FW; no increase in frequency of digestive gland lesions	29
North Carolina, soft parts		
Marina sites	36.7 FW	30
Open water sites	7.1 FW	30
At 12 ‰ salinity	6.0 FW	31
At 33 ‰ salinity	2.0 FW	31
Soft parts		
Alabama	20 (4-78) FW	1
Chesapeake Bay	(5-240) FW	1
Eastern USA	91 (7-517) FW	1
Georgia	(48-261) DW	1
Gulf of Mexico states	16 (6-27) FW	1
Maryland (green oysters)	Max. 1,120 DW	1
NW Atlantic	46 (11-110) DW	1
Rhode Island	121 (92-140) FW	1
Texas	161 DW	1
Virginia; 1972-73		
At 7.5 ‰ salinity	29 FW	31
At 9.5 ‰ salinity	16 FW	31
At 12 ‰ salinity	12 FW	31
At 13.5 ‰ salinity	3 FW	31
Zebra mussel, *Dreissena polymorpha*; soft parts; caged for 15-60 days; water contained 0.8-1.4 µg Cu/L and particulates had 0.3-3.2 µg Cu/L	12.6-17.7 DW	32

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Freshwater mussels; two species; soft parts; St. Lawrence River; 1989-90; sediment copper ranged from 4 to 148 mg/kg DW	7.8-16.2 DW	33
Octopus, *Eledone cirrhosa*; English Channel; October 1987		
Branchial hearts	335 DW	34
Digestive gland	448-463 DW	34
Genital tract	60-66 DW	34
Gill	268 DW	34
Kidney	594 DW	34
Mantle	102 DW	34
Muscle	17 DW	34
Whole	122 DW	34
Mud snail, *Ilyanassa obsoleta*; soft parts; North Carolina		
Marina sites	402.2 FW	30
Open water sites	219.5 FW	30
Baltic clam, *Macoma balthica*; soft parts; The Netherlands; 1990-92		
Acid-soluble fraction	4.1 (2.7-6.7) DW	35
Total copper	13.8-22.6 DW	35
Lagoon mussel, *Mytella strigata*; soft parts; Baja California, Mexico; 1989-91	Max. 3.9 DW	36
Common mussel, *Mytilus edulis*		
Shell		
California	(<5.8-8.6) DW	1
England	9.6 DW	1
Japan	(1.2-2.8) DW	1
New Zealand	3.0 DW	1
Soft parts		
California	(5.0-11.2) DW	1
Canada, Halifax	13.7-154.3 DW	39
England	(7-11) DW	1
Long Island Sound, New York		
1983	1.0-2.3 FW	38
1986-87	15 DW	37
Norway	(3.0-130.0) DW	1
Portugal and Spain	(6.5-14.0) DW	1
Mussel, *Mytilus smarangdium*; soft parts; copper-contaminated environment vs. 6 days in clean seawater	20.2 DW vs. 1.8 DW	28
Mussels; *Mytilus* spp.; soft parts; United States; 1970's vs. 1980's		
Bodega Bay, California	6.9 DW vs. 7.7 DW	40
Narragansett Bay, Rhode Island	11.0 DW vs. 14.0 DW	40
Octopus, *Octopus vulgaris*; hepatopancreas	4,880 DW	1
Squid, *Ommastrephes bartrami*; liver	195 (17-696) DW	1
Clam, *Paphia undulata*; soft parts; Malaysia; 1993	0.9-1.1 FW	20

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Scallop, *Pecten jacobeus*; Adriatic Sea; June 1988		
Digestive gland	16.6 DW	18
Gills	6.3 DW	18
Gonad	10.3 DW	18
Kidney	17.5 DW	18
Mantle	3.3 DW	18
Muscle	1.1 DW	18
Green-lipped mussel, *Perna viridis*; Hong Kong; soft parts; March 1986	Max. 35.1 DW	41
Tropical rock oyster, *Saccostrea cucullata*; soft parts		
Australia, 1983-84; near sewage discharge vs. reference site	285 DW vs. 34 DW	42
Hong Kong, March 1986	Max. 556 DW	41
Sydney rock oyster, *Saccostrea commercialis*; soft parts; Georges River, Australia; 1970's vs. 1980's	20-46 FW vs. 14-93 FW	43
Cuttlefish, *Sepia officinalis*; English Channel; October 1987		
Branchial hearts	256 DW	34
Digestive gland	313-317 DW	34
Genital tract	55-56 DW	34
Gill	183 DW	34
Kidney	185 DW	34
Mantle	141 DW	34
Muscle	9 DW	34
Whole	59 DW	34
Freshwater clam, *Sphaerium* sp.; soft parts; Illinois	10.1 DW	1
Squid, *Symplectoteuthis oualaniensis*; liver	1,720 DW	1
Freshwater mussel, *Unio* sp.; soft parts	11.9-19.3 DW	32
Aquatic arthropods		
Amphipods, various species; whole; Antarctica; 1989	31.3 (30.7-32.0) DW	44
Crayfish, *Astacus astacus*; raw vs. cooked		
Hepatopancreas	52.0 FW vs. 31.0 FW	45
Muscle	5.7 FW vs. 11.0 FW	45
Mayfly, *Baetis thermicus*; whole; larvae; Japan; metal-contaminated river (28.6 µg Cu/L) vs. reference site	73.5 FW vs. 4.0 FW; Cu localized in midgut epithelial cells	46
Crustaceans; 17 species; whole; Antarctic Ocean; 1985-88		
Two species	5.5-7.7 DW	47
Three species	37-42 DW	47
Six species	53-68 DW	47
Four species	81-107 DW	47
Two species	123-149 DW	47
Benthic crab, *Dorippe granulata*; Hong Kong (contaminated harbor)		
Exoskeleton	7.7 DW	48
Gills	123.9 DW	48

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Hemolymph	53.2 FW	48
Midgut gland	114.9 DW	48
Muscle	36.6 DW	48
Euphausiids; Antarctic and Atlantic Oceans; 1985-86; whole		
Euphausia superba	55 (30-86) DW	49
Meganyctiphanes norvegica	58 (40-83) DW	49
Lobster, *Homarus vulgaris*; England		
Blood	32 FW	1
Exoskeleton	3 FW	1
Gill	26 FW	1
Liver	335 FW	1
Muscle	4 FW	1
Ovaries	50 FW	1
Stomach fluid	10 FW	1
Testes	1 FW	1
Urine	2 FW	1
Whole	17 FW	1
Insects; immature benthic species; whole; from copper-contaminated river up to 60 km downstream from outfall (779 mg Cu/kg DW sediments) vs. reference site (18 mg Cu/kg DW sediments)		
Plecoptera	84 DW vs. 16-32 DW	50
Trichoptera	204 DW vs. 11-18 DW	50
Mayflies, four species; whole; nymphs	11-17 DW	1
Beach hopper (amphipod), *Orchestia gammarellus*; whole; North Sea; 1989-90; reference site vs. contaminated site	Usually <70 DW vs. >145 DW (Max. 340 DW)	51
Crayfish, *Pacifasticus leniusculus*; raw vs. cooked		
Hepatopancreas	44 FW vs. 17 FW	45
Muscle	5 FW vs. 8 FW	45
Shrimp, *Pandalus jordani*; muscle	14.3-18.2 DW	1
Brown shrimp, *Penaeus aztecus*; Texas		
Exoskeleton	32 DW	1
Muscle	18-29 DW	1
Whole	34 DW	1
Viscera	173 (65-260) DW	1
Oceanic amphipods, *Themisto* spp; whole; Antarctic and Atlantic Oceans; 1985-86	28-31 (13-79) DW	49
Aquatic annelids		
Polychaete, *Lycastis ouanaryensis*; whole; India; 1984-85; contaminated site vs. reference site	32-95 DW vs. 4-27 DW	52
Tubificid worm, *Tubifex tubifex*; whole; Illinois	23 (10-42) DW	1
Echinoderms		
Sea star (Asteroidea), *Pisaster brevispinus*; California		
Gonad	(2-10) DW	1
Hepatic caecum	(18-38) DW	1

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Stomach	(5-40) DW	1
Tunicates		
Sea squirt, *Ciona intestinalis*		
California		
Tunic	55 DW	1
Viscera	73 DW	1
Sweden, whole	13 DW	1
Elasmobranchs and fishes		
Rockbass, *Ambloplites rupestris*; Ontario, Canada		
Gill	2.1 FW	1
Kidney	3.0 FW	1
Liver	4.9 FW	1
Muscle	1.7 FW	1
Jolthead porgy, *Calamus bajonado*; Puerto Rico		
Eye	1.3 FW; 6.7 DW	1
Gills	1.2 FW; 3.5 DW	1
Intestine	2.4 FW; 10.0 DW	1
Muscle	0.4 FW; 1.5 DW	1
Scales	4.9 FW; 6.9 DW	1
Vertebra	8.3 FW; 14.0 DW	1
Oceanic whitetip shark, *Carcharhinus longimanus*; Puerto Rico		
Liver	1.3 FW; 2.2 DW	1
Muscle	0.5 FW; 2.4 DW	1
Skin	8.6 FW; 21.0 DW	1
Vertebra	3.5 FW; 11.0 DW	1
White sucker, *Catostomus commersoni*; northern Ontario; September 1986; copper-contaminated site (water 9.7 µg Cu/L, sediments 232 mg/kg DW) vs. reference site (2.1 µg/L water, 10 mg/kg DW sediments)		
Feces	208 DW vs. 49 DW	53
Gill	15 DW vs. 6 DW	53
Kidney	26 DW vs. 14 DW	53
Liver	83 DW vs. 50 DW	53
Stomach Contents	155 DW vs. 7 DW	53
Blackfin icefish, *Chaenocephalus aceratus*; Antarctica; 1989		
Liver	4.5 FW	44
Muscle	1.5 DW	44
African sharp-tooth catfish, *Clarias gariepinus*; South Africa; 1988-89; metals-contaminated lake (sediments 216 mg Cu/kg DW)		
Muscle, body fat, vertebra, gonads	9-15 DW	54
Intestine, spleen, liver, kidney, heart, gills	26-46 DW	54
Brain	100 DW	54
Lake whitefish, *Coregonus clupeaformis*; liver, Lake Superior vs. Lake Michigan	2.4 FW vs. 8.5 FW	1
Bloater, *Coregonus hoyi*; liver; Lake Superior vs. Lake Michigan	2.4 FW vs. 7.4 FW	1

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Spotted seatrout, *Cynoscion nebulosus*; whole; South Carolina; 1990-93	0.03-2.9 FW (0.0-19.0) FW	55
Adriatic anchovy, *Engraulis encrasicolus*		
Liver	3.9 FW	1
Muscle	0.7 FW	1
Whole	1.1 FW	1
Northern pike, *Esox lucius*; Ontario		
Gill	1.9 FW	1
Kidney	2.6 FW	1
Liver	10.9 FW	1
Freshwater fishes; Lake Tanganyika, Burundi; two commercially important species *Lates* sp., *Stolothrissa* sp.)		
Gonads	2.0 DW	56
Heart	2.9 DW	56
Intestine	3.2 DW	56
Liver	11.9 DW	56
Muscle	1.7 DW	56
Whole	3.2 DW	56
Freshwater fishes; Tennessee; muscle	0.1-0.9 FW; Max. 2.2 FW	58
Freshwater fishes; USA, nationwide; whole; 8 species		
1984	0.65 FW; Max. 23.1 FW	57
1980-81	0.65 FW; Max. 24.1 FW	57
1978-79	0.82 FW; Max. 38.7 FW	57
Mummichog, *Fundulus heteroclitus*; whole		
Body length 40-51 mm	59 AW	132
Body length 54-121 mm	45-49 AW	132
Atlantic cod, *Gadus morhua*; Norway		
Gill	(4-19) DW	1
Liver	(8-18) DW	1
Muscle	(1-3) DW	1
Brown bullhead, *Ictalurus nebulosus*; Ontario, Canada		
Gill	1.8 FW	1
Kidney	2.5 FW	1
Liver	30.3 FW	1
Muscle	1.3 FW	1
Dab, *Limanda limanda*; liver; German Bight; March 1990; males vs. females	4.3-10.4 FW vs. 5.5-16.0 FW	130
Black marlin, *Makaira indica*; Australia		
Liver	4.6 (0.5-22.0) FW	1
Muscle	0.4 (0.3-1.2) FW	1
Blue marlin, *Makaira nigricans*; muscle		
Japan	0.4 (0.1-0.7) FW	1
Puerto Rico	1.3 (0.4-2.6) FW; 2.7 (1.5-10.0) DW	1
Red mullet (Mullidae), *Mullus barbatus*; gills; Coutou, France	17.6-48.1 DW	59

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Hump rock cod (Notothenidae), *Notothenia gibberifrons*; Antarctica; 1989; muscle	0.85 DW	44
Kelp bass, *Paralabrax clathratus*; California; Los Angeles site near effluent discharge of steam utility plant vs. Catalina Island (reference site)		
Eyeball	8.0 DW vs. 4.0 DW	1
Gonad	6.0 DW vs. 5.0 DW	1
Heart	1.5 DW vs. 12.0 DW	1
Liver	5.0 DW vs. 6.0 DW	1
Muscle	5.0 DW vs. 2.0 DW	1
Southern flounder, *Paralichthys lethostigma*; South Carolina; 1990-93; whole	1.1-1.9 (0.0-22.2) FW	55
Yellow perch, *Perca flavescens*; Michigan; 1993; Torch Lake (34 µg Cu/L) vs. reference site (10 µg Cu/L)		
Ovaries	5.0 DW vs. 2.1 DW	60
Testes	3.5 DW vs. 1.3 DW	60
Southern mouth brooder, *Pseudocrenilabrus philander*; South Africa; whole fish; mine-polluted impoundment	9 (4-26) DW	61
Winter flounder, *Pleuronectes americanus*		
New York		
Muscle	(0.5-1.1) FW	1
Liver	(2.7-13.8) FW	1
Texas		
Muscle	1.0 (0.6-1.5) DW	1
Skin	1.7 (1.2-2.1) DW	1
Atlantic guitarfish, *Rhinobatos lentiginosus*		
Liver	6.6 DW	1
Muscle	2.2 DW	1
Stomach	6.2 DW	1
Red drum, *Sciaenops ocellatus*; South Carolina; 1990-93; whole	0.4-9.2 (0.0-52.9) FW	55
Spanish mackerel, *Scomberomorus maculatus*		
Liver	3.3 DW	1
Muscle	2.3 DW	1
Painted comber, *Serranus cabrilla*; gills; Coutou, France	5.3-27.2 DW	59
Sharks, 10 species; British and Atlantic waters; 1984-88		
Gills	0.05-2.2 FW	62
Gonads	0.1-4.9 FW	62
Heart	0.03 FW	62
Jaws	1.7-3.3 FW	62
Kidney	0.02-4.0 FW	62
Liver	0.2-7.8 FW	62
Muscle	0.2-2.4 FW	62
Pancreas	0.7 FW	62
Skin	0.6-12.1 FW	62
Spleen	0.03-2.5 FW	62

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Vertebra	0.5-5.9 FW	62
Spiny dogfish, *Squalus acanthias*		
Liver	4.5 DW	1
Muscle	2.3 DW	1
Spleen	16.0 DW	1
Bluefin tuna, *Thunnus thynnus*; Spain		
Heart	4.2 FW; 18.1 DW	1
Intestine	1.4 FW; 5.8 DW	1
Kidney	8.6 FW; 27.8 DW	1
Liver	74.0 FW; 245.0 DW	1
Ovary	(1.4-2.3) FW; (5.4-11.0) DW	1
Spleen	1.2 FW; 4.4 DW	1
Red hake, *Urophycis chuss*		
Liver	(3.2-6.0) FW	1
Muscle	(0.5-0.7) FW	1
Swordfish, *Xiphias gladius*; muscle	(0.3-1.4) FW	1
Amphibians and reptiles		
Frogs; Maryland, 1990-91; tadpoles		
Northern cricket frog, *Acris crepitans*; whole	9.8-15.7 DW	131
Gray treefrog, *Hyla versicolor*; whole	7.4-12.6 DW	131
Green frog, *Rana clamitans*		
Gut vs. remainder	21.5 DW vs. 6.7 DW	131
Frogs and toads; Yugoslavia; liver; near mercury mines		
European toad, *Bufo bufo*	56.2-81.4 FW	1
Toad, *Bombina variegata*	(5.0-5.6) FW	1
European frog, *Rana temporaria*	318.9 FW	1
Giant toad, *Bufo marinus*; liver		
Australia	Max. 1,640 DW	63
Dominican Republic		
Black livers	1,248-2,091 DW	63
Yellow livers	367-469 DW	63
American crocodile, *Crocodylus acutus*; egg; Florida	(0.9-15.0) FW	1
Birds		
Western grebe, *Aechmophorus occidentalis*; Puget Sound, Washington; 1985-86; sediments had 52 mg Cu/kg DW		
Diet (fish muscle)	0.3-0.5 FW	64
Liver	12.7-17.6 DW	64
Mallard, *Anas platyrhynchos*; Canada; 1975; feathers; near smelter vs. reference site	23 DW vs. 7-14 DW	65
Black duck, *Anas rubripes*		
Canada; 1975; feathers; near smelter vs. reference site	53 DW vs. 10 DW	65
Ducks, *Anas* spp.; Poland; 1988-91		
Kidney	9.9 (3.5-30.0) FW	66
Liver	58.0 (11.0-200.0) FW	66
Muscle	4.5 (2.1-10) FW	66

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Geese, *Anser* spp.; Poland; 1988-91		
Liver	80 (29-160) FW	66
Muscle	4.0 (1.6-8.8) FW	66
Antarctica; February-March 1989		
Blue eyed cormorant, *Phalacrocorax atriceps*; muscle	10 DW	67
Southern giant petrel, *Macronectes giganteous*; muscle	7.2 DW	67
Adelie penguin, *Pygoscelis adeliae*		
Liver	11.9 (11.0-12.6) DW	67
Muscle	7.9 (6.5-8.5) DW	67
Chinstrap penguin, *Pygoscelis antarctica*		
Feces	37.6 (35.1-49) DW	67
Liver	12.6 (12-13) DW	67
Muscle	9.7 (9.5-10.1) DW	67
Gentoo penguin, *Pygoscelis papua*		
Liver	26.5 (24.0-27.6) DW	67
Muscle	8.2 (7.7-8.9) DW	67
Redhead, *Aythya americana*; Louisiana and Texas; 1987-88; liver	7.3 (3.9-11.5) DW	68
Canvasback, *Aythya valisineria*; Louisiana; 1987-88; liver; females	Usually 76-187 DW	69
Ruffed grouse, *Bonasa umbellus*; liver	5.2 FW	3
Lesser kestrel, *Falco naumanni*; nonviable eggs; Spain; 1988-91	3.1 (0.2-7.1) FW	3
Bald eagle, *Haliaeetus leucocephalus*; eggs		
Florida	(0.7-1.2) FW; (4.8-8.0) DW	1
Maine	(0.3-0.6) FW; (2.0-5.0) DW	1
Wisconsin	(0.5-1.2) FW; (3.0-9.0) DW	1
Willow ptarmigan, *Lagopus lagopus*; Norway; winter 1986-87; kidney; adults vs. juveniles	2.8-4.9 FW (Max. 8.0 FW) vs. 1.9-3.6 FW (Max. 5.5 FW)	71
Lesser black-backed gull, *Larus fuscus*		
Egg	1.0 FW	1
Kidney	14.0 DW	1
Liver	17.0 DW	1
Muscle	14.0 DW	1
Marine birds, New Zealand; 1975-83		
Albatrosses, eight species; adults vs. juveniles		
Feather	44.0 FW vs. 18.4-32.3 W	72
Liver	5.0-8.6 FW vs. 12.2-225.3 FW	72
Gulls, *Larus* spp.; adults vs. juveniles		
Feather	13.1-20.0 FW vs. 25.3-60.5 FW	72
Liver	5.0-6.6 FW vs. 23.8-35.0 FW	72
Penguins, three species; liver; adults vs. juveniles	4.3-13.2 FW vs. 8.5-18.5 FW	72
Petrels, 19 species; adults vs. juveniles		
Feather	14-40 FW vs. 20-79 FW	72
Liver	4-45 FW vs. 8-75 FW	72
Shearwaters, three species of *Puffinus*; liver; adults vs. juveniles	6.4-7.2 FW vs. 4.6-446.3 FW	72

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Surf scoter, *Melanitta perspicillata*; San Francisco Bay; 1985; liver; January vs. March	37.8 (29.3-47.0) DW vs. 50.1 (41.3-58.3) DW	73
Turkey, *Meleagris gallopavo*; Poland; 1988-91		
Kidney	3.0 (2.3-5.2) FW	66
Liver	4.7 (3.1-13.0) FW	66
Muscle	0.3 (0.2-0.4) FW	66
Brown pelican, *Pelecanus occidentalis*		
Egg		
Florida	(0.9-1.1) FW	1
South Carolina	(0.7-1.3) FW	1
Liver; Florida, Georgia, South Carolina	(4.3-9.0) FW	1
Flamingo, *Phoenicopterus ruber roseus*; France; 1988		
Blood serum, nestlings	0.25 (0.13-0.51) FW	74
Feather, adults	Max. 7.43 DW	74
Seabirds, 19 species; pelagic; North Pacific Ocean; 1982-87		
Kidney	4.7 FW	75
Liver	5.9 FW; Max. 7.7 FW	75
Muscle	5.1 FW	75
Shorebirds; Chile; November 1981-March 1982; near abandoned copper mine; liver vs. stomach contents		
Sanderling, *Calidris alba*	(9.2-11.5) FW vs. no data	76
Oyster catcher, *Haematopus ostralegus*	8.0 (6.8-8.6) FW vs. (24.4-27.2) FW	76
Kelp gull, *Larus dominicanus*	(3.8-6.3) FW vs. (0.8-3.4) FW	76
Grey gull, *Larus modestus*	6.2 (4-7.4) FW vs. (30-46.7) FW	76
Franklin's gull; *Larus pipixcan*	(4.7-5.5) FW vs. no data	76
Whimbrel, *Numenius phaeopus*	(3.9-17.8) FW vs. (6.1-86.4) FW	76
Eider, *Somateria mollissima*; Norway		
Egg	4.0 DW	1
Kidney	43.0 DW	1
Liver	367.0 DW	1
Muscle	13.0 DW	1
Tree swallow, *Tachycineta bicolor*; nestlings; acidified (pH 4.8) vs. reference (pH 6.7) lakes; Ontario, Canada; 1986-89		
Kidney	12.8 DW vs. 10.4 DW	77
Liver	42.6 DW (elevated metallothionein) vs. 17.3 DW	77
Redshank, *Tringa totanus*; liver; feeding on sandworms (*Nereis diversicolor*) containing 500-1,000 mg Cu/kg DW	30 DW	78
Marine mammals		
Gray whale, *Eschrichtius robustus*; stranded along North American west coast; 1988-91		
Brain	2.4 FW	79
Kidney	2.4 (0.5-4.9) FW	79
Liver	9.2 (0.6-25.0) FW	79
Stomach contents	21.0 (3.0-66.0) FW	79

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Pilot whale, *Globicephala melaena*; stranded on Cape Cod, Massachusetts, 1986-90		
Adults		
Brain	9.1 (5.7-12.3) DW	80
Kidney	14.7 (7.4-21.0) DW	80
Liver	15.5 (9.9-20.3) DW	80
Ovary	5.5 (2.8-8.4) DW	80
Fetuses		
Brain	5.1 (4.4-6.2) DW	80
Kidney	20.0 (8.1-28.1) DW	80
Gray seal, *Halichoerus grypus*; British Isles and vicinity; 1988-89		
Blubber	<0.1 FW	81
Kidney	(3.2-27.0) FW	81
Liver	(4.0-26.0) FW	81, 82
Muscle	2.5 FW	81
Leopard seal, *Hydrurga leptonyx*; Antarctic; 1989		
Kidney	32.6 (22.5-43.8) DW	83
Liver	105.0 (98.0-116.0) DW	83
Muscle	4.0 (2.5-8.4) DW	83
Stomach contents	14.4 (13.3-16.4) DW	83
Pygmy sperm whale, *Kogia breviceps*; Argentina; found dead		
Heart	6.9 FW	84
Kidney	7.4 FW	84
Liver	10.3 FW	84
Other tissues	<2.3 FW	84
Weddell seal, *Leptonychotes weddelli*; Antarctic; 1989		
Kidney	22.8 (21.7-24.5) DW	83
Liver	57.4 (28-87) DW	83
Muscle	2.8 (2.1-3.1) DW	83
Crabeater seal, *Lobodon carcinophagus*; Antarctic 1989		
Kidney	25.6 (18.9-39.5) DW	83
Liver	71.1 (42-105) DW	83
Muscle	3.3 (2.7-4.3) DW	83
Harbour seal, *Phoca vitulina*; British Isles; 1988-89; liver	7-21 FW	82
Common harbour porpoise, *Phocoena phocoena*		
England; 1988-89; liver	6-160 FW	82
Greenland; 1988-89		
Kidney	5.5 (3.7-8.0) FW	85
Liver	12.0 (5-50) FW	85
Muscle	2.0 (1.1-5.4) FW	85
Skin	1.0 (0.6-1.9) FW	85
Whales; unidentified; 1989; found dead		
Blubber	0.2-1.7 FW	81

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Liver	6.6-8.7 FW	81
Muscle	3.0 FW	81
La Plata river dolphin, *Pontoporia blainvillei*; Argentina; found dead		
Kidney	14 FW	84
Liver	16 FW	84
Other tissues	<2.8 FW	84
Striped dolphin, *Stenella coeruleoalba*; Wales; 1989; found dead		
Blubber	0.3-0.7 FW	81
Muscle	2.1 FW	81
Manatee, *Trichechus manatus*; Florida; 1977-81; liver	175.0 (4.4-1,200.0) DW	86
Dolphin, *Tursiops gephyreus*; Argentina; found dead		
Blubber	4.0 FW	84
Kidney	29.5 FW	84
Liver	77.7 FW	84
Melon	2.7 FW	84
Muscle	6.3 FW	84
Stomach contents	1.2 FW	84
Bottlenose dolphin, *Tursiops truncatus*		
England; 1988-89; liver	4-12 FW	82
Wales; 1989		
Blubber	0.9-1.1 FW	81
Muscle	2.5 FW	81
Polar bear, *Ursus maritimus*		
Canada, Northwest Territories; 1982-84; liver	81-146 DW	87
Svalbard (Arctic Ocean region); 1978-89; adults vs. juveniles		
Kidney	8.3 FW vs. 6.2 FW	88
Liver	42 FW vs. 33 FW	88
Welsh coast and Irish Sea; adults of 17 species of marine mammals; found dead; 1989-91; liver	Usually between 3.2 and 30.0 FW	89
Terrestrial mammals		
Impala, *Aepyceros melampus*; Kruger National Park, South Africa; 1989		
Kidney	(3-141) FW	90
Liver	(3-444) FW	90
Moose, *Alces alces*		
Alaska		
Hair	(5.2-11.7) DW	1
Hoof	(3.2-5.3) DW	1
Estonia; 1980-82		
Kidney	5.1 FW	91
Liver	3.1 FW	91
Poland; 1977-87; muscle	(0.9-2.6) FW	91
Sweden; 1979-80		
Kidney	(2.2-7.4) FW	91

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Liver	(3.2-96.0) FW	91
Arctic fox, *Alopex lagopus*; Norway; 1984-86; liver	6.0 (2.4-26.0) FW	92
Wood mouse, *Apodemus sylvaticus*		
Kidney	(3.7-6.0) FW	1
Liver	(2.6-18.1) FW	1
Testes	(12.2-18.7) FW	1
Whole	(2.8-5.5) FW	1
Bison, *Bison bison*; Canada; 1986		
Kidney	6.7 (5.5-8.0) FW	91
Liver	35 (13-52) FW	91
European bison, *Bison bonasus*; Poland; 1987		
Kidney	4.4 FW	91
Liver	3.4 FW	91
Muscle	2.0 FW	91
Cattle, *Bos* spp.		
Poland; 1987-91		
Kidney	5.6 FW	93
Liver	29.0 FW	93
Muscle	1.2 FW	93
South Africa; 1989; found dead near copper smelter; surface soil had 103 mg Cu/kg DW (14 at reference site)		
Kidney	36 (6-83) FW; 108 DW	90
Liver	359 (161-600) FW; 1,078 DW	90
Various locations; liver	38.2-156.1 DW	94
Water buffalo, *Bubalus* sp.; Kruger National Park, South Africa; 1989; liver	Usually 18-80 FW; (6-144) FW	90
Bactrian camel, *Camelus bactrianus*; China; 1992		
Normal		
Blood	0.86 FW	95
Hair	6.4 DW	95
Camels with sway disease (severe copper deficiency)		
Nonpregnant females		
Blood	0.36 FW	95
Hair	4.3 DW	95
Pregnant camels vs. post-partum		
Blood	0.17 FW vs. 0.26 FW	95
Hair	3.0 DW vs. 3.3 DW	95
Dog, *Canis familiaris*		
Brain	3.9 FW; 19 DW	96
Kidney	6.9 FW; 26 DW	96
Liver	82 FW; 336 DW	96
Muscle	1.1 FW; 3.7 DW	96
Serum	0.7 FW	96
Whole body	2.3 FW	96
Coyote, *Canis latrans*; kidney	5.2 FW	97

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Goat, *Capra hircus*; mother vs. newborn		
Hair	8.9 DW vs. 8.3 DW	1
Kidney	9.8 DW vs. 19.0 DW	1
Liver	11.3 DW vs. 63.3 DW	1
Roe deer, *Capreolus capreolus*; Poland; 1987-91		
Kidney	7.8 FW	91
Liver	28.0 FW	91
Muscle	4.5 FW	91
European red deer, *Cervus elaphus*		
The Netherlands; 1989-92		
Kidney	54-86 DW	98
Liver	14-18 DW	98
Poland; 1986-91		
Kidney	5.4 FW	91
Kidney	9.4 DW	99
Liver	12.0 FW	91
Muscle	6.3 FW	91
Muscle	19.0 DW	99
Bank vole, *Clethrionomys glareolus*		
Poland; 1990; whole, less stomach and gastrointestinal tract	5.7-9.5 DW	100
Poland; 1985; various sites		
Bone	18.2-22.7 DW	101
Fur	12.0-14.5 DW	101
Kidney	43.4-73.8 DW	101
Liver	27.6-31.2 DW	101
Remainder	12.5-28.8 DW	101
Horse, *Equus caballus*; liver	10.3-51.5 DW	94
North American porcupine, *Erethizon dorsatum*		
Heart	8.4 FW	97
Lung	4.7 FW	97
Human, *Homo sapiens*		
Healthy adults vs. adults with Wilson's Disease		
Bone	2.9 FW vs. 31.0 FW	58
Brain	5.4 FW vs. 54.9 FW	58
Cornea	3.8 FW vs. 35.1 FW	58
Kidney	2.8 FW vs. 36.2 FW	58
Liver	7.8 FW vs. 99.2 FW	58
Normal adults		
Aorta	82-280 AW	97
Blood	1.0 FW	102
Brain	310-540 AW	97
Hair	31 DW	102
Heart	310-420 AW	97
Kidney	220-880 AW	97
Liver	480-2,000 AW; 10 FW	58, 97
Lung	140-470 AW	97

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Pancreas	96-310 AW	97
Serum	1.64 FW	102
Spleen	93-470 AW	97
Whole body	1.4 (1.0-1.7) FW	58, 102
Fetus (33 weeks)	22.0 FW	103
Full term (still birth)	37.9 FW	103
Newborn, whole	4.0 FW	102
Diet, adults		
Beverages	0.44 FW	97
Condiments	6.8 FW	97
Dairy products	1.8 FW	97
Most fruits	0.82 FW	97
Coconut seed	3.3 FW	97
Most grains and cereals	2.0 FW	97
Grapenuts®	15.0 FW	97
Meats	3.9 (0.95-11.0) FW	97
Beef liver	11.0 FW	97
Nuts	14.8 FW	97
Most oils and fats	4.6 FW	97
Lecithins	21.0 FW	97
Most seafoods	1.5 (0.5-3.4) FW	97
Oysters	137.1 FW	97
Most vegetables	1.2 FW	97
Peas, split, green, dry	12.3 FW	97
Woodchuck, *Marmota monax*; liver	9.4 FW	97
Mice, *Mus* spp.		
Fat	2.4 FW	97
Kidney	3.8 FW	97
Liver	2.0 FW	97
Lung	3.9 FW	97
Deer, *Odocoileus* spp.		
Brain	0.3-2.4 FW	97
Hooves	0.6 FW	97
Kidney	5.8-8.4 FW	97
White-tailed deer, *Odocoileus virginianus*; Texas; 1979-80; uranium mining district vs. reference site		
Antlers	16.7 (0.5-71.0) FW vs. 18.0 (0.6-94.0) FW	104
Liver	0.5-94.0 FW vs <1.0->70.0 FW	104
Muskrat, *Ondatra zibethicus*; Virginia; 1986-88; contaminated site (many chemicals; 68 mg Cu/kg DW sediment) vs. reference site (26 mg Cu/kg DW sediment); kidney	12.9 DW vs. 11.1 DW	105
Rabbit, *Oryctolagus* sp.; Poland; 1990; industrialized area vs. reference site		
Heart	5.9 FW vs. 3.0 FW	106
Kidney	6.6 FW vs. 2.6 FW	106
Liver	5.8 FW vs. 3.1 FW	106
Muscle	2.4 FW vs. 1.2 FW	106

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Muskox, *Ovibus moschatus*; Canadian Arctic; 1985-90		
Kidney	11 DW	107
Liver	67 DW	107
Domestic sheep, *Ovis aries*		
Copper-poisoned vs. normal sheep		
Blood	1.74-9.1 FW vs. 0.6-1.6 FW	108
Kidney	60 FW vs. 5 FW	109
Liver	432 FW vs. 12 FW	109
Muscle	2.5 FW vs. 2.1 FW	109
Spleen	19 FW vs. 5 FW	109
England; in paddock near heavily traveled highway for 150 days vs. reference site		
Blood	0.98 FW vs. 0.97 FW	110
Wool, tip	28.6 DW vs. 12.4 DW	110
Poland; 1988-91		
Kidney	5.7 (3.1-13.0) FW	66
Liver	41 (7-98) FW	66
Muscle	0.9 (0.8-1.3) FW	66
Raccoon, *Procyon lotor*; fat	1.2 FW	97
Caribou, *Rangifer tarandus*; Canadian Arctic; 1985-90		
Kidney	29 DW	107
Liver	68 DW	107
Rat, *Rattus* spp.		
Mature and aged		
Brain	6.6 FW	97
Heart	1.0 FW	97
Kidney	0.9 FW	97
Liver	0.7 FW	97
Lung	0.9 FW	97
Spleen	0.3 FW	97
Tumors		
Hepatic	2.5 FW	94
Ovarian	5.9 FW	97
Mammarian	1.3 FW	97
Young, whole	0.52 FW	97
Gray squirrel, *Sciurus carolinensis*; liver	4.8 FW	97
Shrews, *Sorex* spp.; England; 3 km from lead-zinc smelter vs. 23 km		
Carcass		
Immature	21.2 DW vs. 11.9 DW	111
Mature	21.7 DW vs. 13.1 DW	111
Kidney		
Immature	19.2 DW vs. 6.5 DW	111
Mature	13.6 DW vs. 8.8 DW	111
Liver		
Immature	32.5 DW vs. 14.8 DW	111
Mature	23.3 DW vs. 22.9 DW	111

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Rock squirrel, *Spermophilus variegatus*		
Bone	(4.0-7.8) DW	1
Liver	(12.1-24.1) DW	1
Wild boar, *Sus scrofa*		
Germany; 1988; near metal foundry vs. reference site; liver	20.0 (10.9-49.6) FW vs. 15.9 (5.7-26.7) FW	112
The Netherlands; 1989-92; kidney vs. liver	17-24 DW vs. 4-20 DW	
Poland, 1986-91		
Kidney	1.7 FW; 17.2-24.5 DW	91, 99
Liver	1.8 FW	91
Muscle	1.6 FW; 6.4-7.4 DW	91, 99
Swine, *Sus* sp.; Poland; 1987-91		
Kidney	8.4 (2.1-44.0) FW	113
Liver	8.5 (1.1-41.0) FW	113
Muscle	1.1 (0.1-14.0) FW	113
Red fox *Vulpes vulpes*; liver	41.8 FW	97
Integrated studies		
Canada; northern Ontario; August 1988; Lake Manitouwadge (contaminated) vs. Lake Wowun (reference site)		
Sediments	93 DW vs. 3 DW	114
Water (soluble copper)	0.015 FW vs. 0.002 FW	114
Invertebrates	89 DW vs. 57 DW	114
White sucker, *Catostomus commersoni*		
Bone	4 DW vs. 3 DW	114
Digestive tract	107 DW vs. 16 DW	114
Gill	9 DW vs. 3 DW	114
Kidney	31 DW vs. 10 DW	114
Liver	98 DW vs. 46 DW	114
Muscle	5 DW vs. 3 DW	114
Ovary	13 DW vs. 8 DW	114
Testes	10 DW vs. 2 DW	114
Canada; Sudbury, Ontario; 1970		
Soils; distance from smelter		
0.8-1.9 km	940-2,070 DW	115
7.4-13.5 km	940-1,620 DW	115
49.8 km	20-30 DW	115
Red maple, *Acer rubrum*; foliage; distance from smelter		
1.6 km	37 DW	115
6.5-18 km	19-28 DW	115
Wavy hairgrass, *Deschampia flexuosa*; distance from smelter		
1.6 km	726 DW	115
7.4 km	103 DW	115
49.8 km	13 DW	115
Lowbush blueberry, *Vaccinium angustifolium*; foliage; distance from smelter		
1.6 km	75 DW	115

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
4.6 km	35 DW	115
6.5-31 km	14-22 DW	115
India; river near Madras; receives industrial wastes		
Sediments	760-930 DW	116
Water	0.01-0.04 FW	116
Alga, *Enteromorpha intestinalis*; whole	12.3 FW	116
Oyster, *Crassostrea madrasensis*; soft parts	4.2 FW	116
Crustaceans, whole	Max. 18.4 FW	116
Fishes, muscle	Max. 0.09 FW	116
Israel; Acre Valley; 1988-91		
Mollusks; soft parts		
Bivalves	9.4-13.3 DW	117
Gastropods	31.0-48.0 DW	117
African sharp-tooth catfish, *Clarias gariepinus*; liver	Max. 92.0 DW	117
Italy; Goro Bay; 1991-92		
Sediments	42-54 DW	118
Seawater	0.0005-0.0022 FW	118
Mussel, *Mytilus galloprovincialis*; soft parts; purged for 48 h in aerated synthetic seawater vs. not purged	6.9 DW vs. 13.1 DW	118
New Zealand; pasture soil contaminated by runoff from an adjacent timber treatment plant; 1993; copper-contaminated soils (70-1,233 mg Cu/kg DW soil) vs. reference site (25 mg Cu/kg DW soil)	In less-contaminated soils, plant-feeding nematodes were predominant. With increasing copper loadings, bacterial-feeding and predatory nematodes dominated; at highest loadings, microbial biomass declined	119
New Zealand; pasture contaminated by runoff from chromated copper arsenate timber preservation facility; 1991; control surface soils contained an average of 19 mg Cu/kg DW, low contamination 109 mg/kg, medium contamination 425 mg/kg, and high contamination 835 mg/kg DW soil		
Vegetation	Herbage yield decreased with increasing copper loadings; after 35 days roots had 10.5 mg Cu/kg DW in controls, 14.6 in low group, 18.4 in medium group and 23.9 in high group	120
Earthworms, *Lumbricus rubellus, Aporrectodea rosea*	Earthworms absent from plats with medium and high contamination. Surface casts of *L. rubellus* had 17.5 mg/kg DW in low contamination soils vs. 7.0 in controls; for *A. rosea* these values were 13.3 vs. 7.0	120
Nematodes	Most abundant in low-contamination soils; proportion of predatory nematodes in population increased with increasing copper contamination	120
Soil microflora	Reduced with increasing contamination	120
Norway; small lakes; 1991; near highway vs. reference site		
Freshwater mussel, *Anodonta piscinalis*; soft parts	3.5 FW vs. 3.1 FW	121
Perch, *Perca fluviatilis*		
Liver	1.6 FW vs. 1.5 FW	121
Muscle	0.16 FW vs. 0.19 FW	121

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
South Africa; metal-polluted wetland; 1989		
Sediments	67.4 (44.3-93.3) DW	122
Sago pondweed, *Potamogeton pectinatus*; whole	29.0 DW	122
Red-knobbed coot, *Fulica cristata*; feeding on *Potamogeton pectinatus*		
Egg contents	8.5 DW	122
Egg shell	5.5 DW	122
Gonads	32.6 (10.8-59.9) DW	122
Internal organs	24.5 (0.4-125.1) DW	122
Stomach contents	37.0 (11.3-90.1) DW	122
Wales; 1989; coastal area		
Sediments	8.0 DW	123
Anemones, whole	0.6 FW	123
Soft corals, whole	1.0 FW	123
Mussels, soft parts	1.2 FW	123
Crab, hepatopancreas	58.0 FW	123
Lugworms, whole	3.9 FW	123
Tunicates, whole	2.6 FW	123
Fishes, four species; liver	1.6-4.4 FW	123
United States; Florida; 1979; national wildlife refuge; treated with copper-containing herbicides vs. nontreated areas		
Water	Max. 0.56 FW after 1 h to 0.04 FW after 24 h vs. 0.027 FW	124
Detritus	Max. 20.1 DW after 7 days vs. 12-13 DW	124
Aquatic plants	Max. 151.3 DW after 14 h vs. 9-10 DW	124
Apple snail, *Pomacea paludosa*; soft parts		
Adults	82.3 DW after 7 days vs. 17-21 DW	124
Immatures	80.3 DW after 7 days vs. 11-22 DW	124
United States; Kansas: 1990; near landfill; upstream vs. downstream site		
Sediments	8.2-17.9 DW vs. 12.4-14.6 DW	125
Water	0.01-0.018 vs. 0.007-0.019 FW	125
Crayfish, *Orconectes nais*; whole	60.3-61.3 DW vs. 56.2-77.7 DW	125
Orangespotted sunfish, *Lepomis humilis*; whole	1.5-7.3 DW vs. 1.4-2.5 DW	125
United States; Maryland and Pennsylvania; 1985; at disposal facilities for dredged materials; low soil copper site (15 mg/kg DW) vs. high soil copper site (150 mg/kg DW)		
Common reed, *Phragmites australis*; whole	2.8 DW vs. 4.7 DW	126
Ladybug, *Coccinella septempunctata*; whole	14 DW vs. 17 DW	126
Earthworms, *Eisenia foetida*; whole	21 DW vs. 57 DW	126
House mouse, *Mus musculus*; whole less skin and tail	13 DW vs. 18 DW	126
United States; Montana; 1990; wetland contaminated by mining wastes (arsenic, cadmium, copper, lead, zinc)		
Soil	532.0 DW	127
Water	0.078 FW	127

Table 3. *Continued.*

Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Vegetation		
Aboveground	7.2-24.2 DW	127
Belowground	75.0-274.0 DW	127
Meadow vole, *Microtus pennsylvanicus*		
Carcass	2.8 FW	127
Kidney	5.1 FW	127
Liver	4.2 FW	127
Testes	1.9 FW	127
Deer mice, *Peromyscus maniculatus*		
Carcass	3.4 FW	127
Kidney	5.7 FW	127
Liver	5.7 FW	127
Testes	1.5 FW	127
United States; Ohio; 1987; old-field community; treated with sewage sludge for 10 years beginning in 1978; treated plots vs. reference site		
Sludge	320-381 DW vs. not applicable	128
Soil	Sludge loading equivalent to 15-37 DW vs. no data	128
Plants, stems		
Japanese brome, *Bromus japonicum*	5.9 DW vs. 6.0 DW	128
Bluegrass, *Poa* spp.	7.4 DW vs. 6.3 DW	128
Raspberry, *Rubus* sp.	4.7 DW vs. 3.4 DW	128
Foxtail, *Setaria* sp.	6.3 DW vs. 2.9 DW	128
Earthworms, *Lumbricus rubellus*	17-23 DW vs. no data	128
Meadow vole, *Microtus pennsylvanicus*		
Kidney	3.3 DW vs. 3.0 DW	128
Liver	3.1 DW vs. 3.5 DW	128
United States; Pennsylvania; Palmerton zinc smelter; 1986 (6 years after smelter was closed); near smelter vs. distant sites		
Soil	190 DW vs. <30 DW	129
Litter	552 DW vs. <70 DW	129
Green frog, *Rana clamitans*; tadpoles; whole	0.8 FW vs. 0.3 FW	129
Eastern red-backed salamander, *Plethodon cinereus*; whole less gastrointestinal tract	2.2 FW vs. 1.7 FW	129
White-tailed deer, *Odocoileus virginianus*		
Bone	11 DW vs. 16 DW	129
Kidney	29 DW vs. 33 DW	129
Liver	122 DW vs. 149 DW	129
Eastern cottontail rabbit, *Sylvilagus floridanus*		
Bone	6.7 DW vs. 6.7 DW	129
Kidney	21.5 DW vs. 17.8 DW	129
Liver	19.2 DW vs. 14.8 DW	129
Muscle	11.9 DW vs. 9.6 DW	129

[a]Concentrations are shown as means, range (in parentheses), maximum (Max.), and nondetectable (ND)

[b]1, Jenkins 1980; 2, NAS 1977; 3, Schroeder et al. 1966; 4, Hutchinson 1979; 5, Jozwik 1990; 6, Reed et al. 1993; 7, Veleminsky et al. 1990; 8, Berger and Dallinger 1993; 9, Lindquist 1993; 10, Heliovaara and Vaisanen 1990; 11, Morgan and Morgan 1990; 12, Clark 1992; 13, Larsen et al. 1994; 14, Karez et al. 1994; 15, Stokes 1979; 16, Brix and Lyngby 1982; 17, Jaffe et al. 1992; 18, Mauri et al. 1990; 19, Viarengo et al. 1993; 20, Mat 1994; 21, Mat et al. 1994; 22, Pip 1990; 23, Balogh and Mastala 1994; 24, Swaileh and Adelung

Table 3. *Continued.*

1994; 25, Cheung and Wong 1992; 26, Claisse and Alzieu 1993; 27, Han and Hung 1990; 28, Han et al. 1993; 29, Weis et al. 1993a; 30, Byers 1993; 31, Huggett et al. 1975; 32, Camusso et al. 1994; 33, Metcalfe-Smith 1994; 34, Miramand and Bentley 1992; 35, Bordin et al. 1994; 36, Paez-Osuna et al. 1994; 37, Turgeon and O'Connor 1991; 38, Greig and Sennefelder 1985; 39, Ward 1990; 40, Lauenstein et al. 1990; 41, Chu et al. 1990; 42, Talbot et al. 1985; 43, Brown and McPherson 1992; 44, Szefer et al. 1993; 45, Jorhem et al. 1994; 46, Sumi et al. 1991; 47, Petri and Zauke 1993; 48, Depledge et al. 1993; 49, Rainbow 1989; 50, Cain et al. 1992; 51, Moore et al. 1991; 52, Athalye and Gokhole 1991; 53, Munkittrick et al. 1991; 54, Bezuidenhout et al. 1990; 55, Mathews 1994; 56, Sindayigaya et al. 1994; 57, Schmitt and Brumbaugh 1990; 58, ATSDR 1990; 59, Romeo et al. 1994; 60, Ellenberger et al. 1994; 61, de Wet et al. 1994; 62, Vas 1991; 63, Goldfischer et al. 1970; 64, Henny et al. 1990; 65, Ranta et al. 1978; 66, Falandysz et al. 1994; 67, Szefer et al. 1993; 68, Michot et al. 1994; 69, Custer and Hohman 1994; 70, Negro et al. 1993; 71, Wren et al. 1994; 72, Lock et al. 1992; 73, Ohlendorf et al. 1991; 74, Amiard-Triquet et al. 1991, 75, Honda et al. 1990; 76, Vermeer and Castilla 1991; 77, St. Louis et al. 1993; 78, Bryan and Langston 1992; 79, Varanasi et al. 1994; 80, Meador et al. 1993; 81, Morris et al. 1989; 82, Law et al. 1991; 83, Szefer et al. 1994; 84, Marcovecchio et al. 1990; 85, Paludan-Muller et al. 1993; 86, O'Shea et al. 1984; 87, Braune et al. 1991; 88, Norheim et al. 1992; 89, Law et al. 1992; 90, Gummow et al. 1991; 91, Falandysz 1994; 92, Prestrud et al. 1994; 93, Falandysz 1993a; 94, Cuill et al. 1970; 95, Zong-Ping et al. 1994; 96, Goresky et al. 1968; 97, Schroeder et al. 1966; 98, Wolkers et al. 1994; 99, Swiergosz et al. 1993; 100, Zakrzewska et al. 1993; 101, Sawicka-Kapusta et al. 1990; 102, USEPA 1980; 103, Bakka and Webb 1981; 104, King et al. 1984; 105, Halbrook et al. 1993; 106, Krelowska-Kulas et al. 1994; 107, Gamberg and Scheuhammer 1994; 108, MacPherson and Hemingway 1969; 109, Todd 1969; 110, Ward and Savage 1994; 111, Read and Martin 1993; 112, Launer et al. 1991; 113, Falandysz 1993b; 114, Miller et al. 1992; 115, Hutchinson 1979; 116, Govindarajan and Rao 1992; 117, Fishelson et al. 1994; 118, Fagioli et al. 1994; 119, Bardgett et al. 1994; 120, Yeates et al. 1994; 121, Baekken 1994; 122, van Eeden and Schoonbee 1993; 123, Morris et al. 1989; 124, Winger et al. 1984; 125, Morrissey and Edds 1994; 126, Beyer et al. 1990; 127, Pascoe et al. 1994; 128, Levine et al. 1989; 129, Storm et al. 1994; 130, Hylland et al. 1992; 131, Sparling and Lowe 1996; 132, Eisler and LaRoche 1972.

In aquatic vegetation, copper is elevated in metals-contaminated water bodies, reaching concentrations as high as 1,350 mg/kg DW in eelgrass (*Zostera* spp.) from contaminated bays vs. 36 mg/kg DW in conspecifics from reference sites (Table 3).

Copper concentrations in terrestrial invertebrates from industrialized areas range from 137 to 408 mg/kg DW. Soil invertebrates are not likely to accumulate copper but are important in recycling copper through terrestrial food webs. Aquatic invertebrates seldom contain as much as 95 mg Cu/kg DW, regardless of collection locale; exceptions include whole amphipods and lobster hepatopancreas (335-340 mg/kg DW) from copper-contaminated sites and many species of mollusks that normally contain 1,100-6,500 mg Cu/kg DW (Table 3).

Maximum concentrations of copper in elasmobranchs and teleosts from all collection sites range from 7-15 mg/kg DW in eyeballs, intestines, muscle, scales, vertebrae, heart, and gonads and from 16-48 mg/kg DW in gills, kidneys, skin, and spleens and reach 53 mg/kg DW in whole animals, 155 mg/kg DW in stomach contents, 208 mg/kg DW in feces, and 245 mg/kg DW in livers (Table 3).

Data on copper concentrations in field collections of amphibians and reptiles are scarce. Crocodile eggs contain as much as 60 mg Cu/kg DW; however, some toads (*Bufo* spp.) may contain as much as 2,100 mg Cu/kg DW in livers without apparent adverse effects (Table 3; Goldfischer et al. 1970).

Birds from contaminated sites may contain as much as 9-28 mg Cu/kg DW in eggs, muscle, and stomach contents; 43-53 mg/kg DW in kidneys, feces, and feathers; and 367 mg/kg DW in livers (Table 3).

Marine mammals usually contain less than 44 mg Cu/kg DW in all tissues except livers. Copper in livers seldom exceeds 116 mg/kg DW except in polar bears (146 mg/kg DW), and manatees, *Trichechus manatus*, (1,200 mg/kg DW) from a copper-contaminated site (Table 3). Maximum copper concentrations in terrestrial mammals from all collection sites are usually less than 29 mg/kg DW in all tissues except kidneys (108 mg/kg DW) and livers (1,078 mg/kg DW; Table 3).

Abiotic Materials

Copper concentrations in abiotic materials are comparatively elevated near copper smelters and urban areas (Table 2). Copper concentrations are also elevated in drinking water from copper pipes, in poultry and livestock manures, mine tailings, fossil fuels, shales (Table 2), sewage sludge, and in wastes from plating industries, foundries, and coking plants (ATSDR 1990). Drinking waters from certain locales contain elevated concentrations of copper added intentionally to control algal growth; drinking water may account for 10-20% of the daily intake of copper in humans (USEPA 1980).

Copper is found in the rocks and minerals of the earth's crust, occurring usually as sulfides and oxides, and sometimes as metallic copper (USEPA 1980). The mean concentration of copper in the upper lithosphere ranges from 70-100 mg/kg, ranking 14th of the trace elements in this compartment (Schroeder et al. 1966). Copper in the environmental crust averages 50 mg/kg, but is higher (140 mg/kg) in ferromagnesium minerals (NAS 1977). Soil contamination by copper occurs around all known smelter locations; contamination may persist for decades, and plants and

animals are often unable to survive the harsh chemical environments created (Hutchinson 1979). Italian soils have higher copper concentrations (51 mg/kg DW) than those of other European countries, probably as a result of the widespread and prolonged application of copper-based fungicides in Italian orchards and vineyards (Arduini et al. 1995).

Copper concentrations in lake sediments within a radius of 80 km from a smelter in northern Sweden are positively correlated with proximity to the smelter (Johnson et al. 1992). In some cases, lake sediments are sinks for copper, with little release to the overlying lake water. For example, copper-bearing mine tailings in Butte Lake, British Columbia, do not undergo oxidative diagenesis because of a rapid rate of accumulation and short exposure time to dissolved oxygen in bottom waters (Pedersen 1983). In Michigan, lakes with elevated concentrations of copper (34 µg/L) have low densities of fish populations (Ellenberger et al. 1994). In the Elizabeth River estuary of southern Chesapeake Bay, anthropogenic copper and other chelatable metals are present at concentrations sufficient to adversely affect growth and survival of the copepod *Acartia tonsa* (Sunda et al. 1990). In Norway, freshwater fish are present only when copper is less than 60 µg/L and some humic acids are present (Hodson et al. 1979). Successful reproduction of the spotted salamander (*Ambystoma maculatum*) occurs at low water concentrations of copper (<10 µg/L), lead, and aluminum, and high concentrations of silicon. Failed reproduction occurs at low water concentrations of silicon, and elevated concentrations of copper (>25 µg/L), lead, and aluminum (Blem and Blem 1991).

In marine ecosystems, the high copper levels measured in heavily contaminated coastal areas sometimes approach the incipient lethal concentrations for some organisms (Neff and Anderson 1977). Elevated copper concentrations in marine and estuarine environments may result from atmospheric deposition, industrial and municipal wastes, urban runoff, rivers, and shoreline erosion. Chesapeake Bay, for example, receives more than 1,800 kg of copper daily from these sources (Hall et al. 1988). Copper concentrations in abiotic marine materials are generally higher near shore than off shore. Copper is elevated in sediments of many marinas, probably from the copper antifouling bottom paints used on boats housed in these marinas (Hall et al. 1988). In New Zealand, copper concentrations in contaminated inshore sediments frequently exceed 100 mg Cu/kg DW vs. 14 mg Cu/kg DW at noncontaminated sites (Roper and Hickey 1994). The fine particle fraction of sediments collected near bulkheads made of chromated copper arsenate (CCA)-treated wood contain elevated concentrations of copper, chromium, and arsenic; metal concentrations decreased with increasing distance from the bulkhead. Sediments, for example, decreased from 11 mg Cu/kg DW in the vicinity of treated bulkheads to less than 2 mg/kg DW at more distant sites (Weis and Weis 1994).

Terrestrial Plants and Invertebrates

In general, copper concentrations in terrestrial vegetation seldom exceed 35 mg/kg DW, except near point sources of copper contamination and in certain copper-tolerant species (Table 3). The highest copper concentration recorded in nonaccumulator plants is 726 mg/kg DW in hair grass (*Deschampsia flexuosa*) near a smelter (Table 3). Several species of terrestrial plants accumulate spectacular concentrations of copper. Mint plants (*Aeolanthus* spp., *Elsholtzia* spp.) growing in copper-rich soils contain unusually high concentrations and are used as economic indicators of copper deposits in the former Soviet Union and the People's Republic of China (Jenkins 1980). The copper plant mint (*Aeolanthus biformifolius*), for example, normally contains as much as 13,700 mg Cu/kg DW whole plant (Table 3). Copper-tolerant species of mosses, lichens, fungi, and higher plants occur in Greenland, Canada, the former Soviet Union, Africa, and elsewhere. In Zambia and Rhodesia, the copper-tolerant *Becium homblei* is found only in soils containing more than 1,000 mg Cu/kg and is believed responsible for the discovery of copper deposits in those nations (Hutchinson 1979). Some species of copper-indicator plants in Zambia tolerate as much as 70,000 mg Cu/kg in the soil and accumulate as much as 3,000 mg Cu/kg in leaves (Hutchinson 1979).

Copper is not accumulated from soils by most crop plants, suggesting a soil-plant barrier for copper (Levine et al. 1989). Thus, corn (*Zea mays*) did not accumulate copper from soils treated with 365 kg of copper per surface hectare (as copper-rich pig manure or copper sulfate) over a 13-year period; corn yield is not affected under these conditions (Reed et al. 1993).

Copper burdens in terrestrial invertebrates are highest in organisms collected near industrial locations and urban areas or from copper-contaminated soils. The highest copper concentration recorded among terrestrial invertebrates is 408 mg Cu/kg DW soft parts in gastropods from urban areas (Table 3). Copper concentrations in pine moths (*Bupalus piniaria*) and pine noctuids (*Panolis flammea*) from industrialized areas range from 89-137 mg/kg DW, but are lower than dietary concentrations and suggest negligible accumulation (Heliovaara and Vaisanen 1990). Accumulations of as much as 60 mg Cu/kg DW in 17-year cicadas (*Magicicada* spp.) pose no apparent dietary threat to insectivorous birds (Clark 1992).

Earthworms from soils heavily contaminated with copper (2,740 mg/kg DW soil) can regulate copper more efficiently than cadmium and lead. However, copper is more toxic to earthworms than lead or zinc in the soil due, in part, to the inability of most soft tissues to synthesize copper-binding ligands when challenged with copper (Morgan and Morgan 1990).

In woodland ecosystems, copper concentrations in the litter horizon are rarely exceeded by those in soil animals—

which play a key role in copper cycling (Wieser 1979). Meiofaunal feces comprise an efficient distributing system through which copper and other nutrients are cycled through the food web of woodland ecosystems. During a 12-month cycle the total copper bound in litter progresses through a cycle of chemical binding states. It may be released from a strongly chelated organic complex as the litter is attacked by the digestive juices of animals or it may be discharged in soluble form with the feces and become complexed again by the activity of microorganisms in these feces. When feces are ingested by coprophagous animals, such as isopods, the copper may become trapped in proteins or membrane-bound vesicles (Wieser 1979).

Aquatic Organisms

Copper is essential for the successful growth and development of many species of aquatic organisms, but its rate and extent of accumulation and retention are modified by numerous biological and abiotic variables. Abiotic variables known to modify copper concentrations in tissues of aquatic biota include water temperature, pH, salinity, and depth; the presence of other inorganics, organics, and chelators; the chemical species of copper; and proximity to anthropogenic point sources of copper. Biological variables affecting copper accumulations in marine organisms include the organism's age, size, and developmental stage; physiological or genetic adaptation to high copper substrates; inherent species differences; and tissue specificity, such as the thorax of barnacles, gill and osphradium of gastropods, and livers of teleosts (Eisler 1979). Among marine organisms, the highest accumulations are generally found in molluskan tissues and soft parts, especially those of cephalopods and oysters. In order of decreasing copper accumulations, mollusks are followed by crustaceans, macrophytes, annelids, tunicates, algae, echinoderms, and coelenterates. Lowest concentrations of copper were consistently found among the vertebrates—elasmobranchs, fishes, mammals—and strongly indicates a discrimination against copper among the highest marine trophic levels examined (Eisler 1979, 1981). Aquatic mollusks and arthropods that possess hemocyanin—a copper-containing respiratory pigment—have elevated tissue and plasma copper concentrations when compared to the ambient medium (Neff and Anderson 1977). Unlike many species of invertebrates, no vertebrate animal has a copper pigment as the main metallic constituent of blood (Schroeder et al. 1966). Marine organisms without hemocyanin have lower tissue concentrations of copper than those possessing this respiratory pigment (Neff and Anderson 1977).

Diet is the most important route of copper accumulation in aquatic animals, and food choice influences body loadings of copper. For example, whole body copper concentrations in aquatic insects from copper-contaminated rivers are highest in detritovores (as high as 102 mg/kg DW), followed by predators (54 mg/kg DW) and omnivores (43 mg/kg DW; Cain et al. 1992). Little or no biomagnification of copper is evident in freshwater food chains (Stokes 1979).

Copper concentrations in freshwater macrophytes near mining areas are elevated (as much as 256 mg/kg DW) compared to conspecifics collected from more remote sites (Stokes 1979). Bioconcentration factors (ratio of milligrams of copper per kilogram fresh weight organism to milligrams of copper per liter of ambient water) for copper by various species of freshwater algae range from 770-83,000. In general, copper accumulations in algae are higher at pH 8 than at pH 5; under conditions of low oxygen and reduced illumination; at low ambient concentrations of calcium, cobalt, zinc, magnesium, manganese, and organic chelators; and at high ambient concentrations of fluoride (Stokes 1979). Benthic communities in the vicinity of bulkheads made of chromated copper arsenate-treated wood had elevated concentrations of these elements, reduced species richness and diversity, and reduced numbers of total organisms when compared to reference sites (Weis and Weis 1994). American oysters (*Crassostrea virginica*) from a canal lined with chromated copper arsenate-treated wood had 150 mg Cu/kg FW soft parts vs. 20 mg Cu/kg FW in oysters from a more distant site (Weis and Weis 1993).

Copper concentrations in cephalopod mollusks are, in general, higher than those in bivalve mollusks; in cephalopods, 50 to 80% of the copper is localized in the digestive gland (Miramand and Bentley 1992). Copper concentrations in tissues of clams *(Macoma balthica)* in San Francisco Bay are associated with seasonal variations in tissue weight, concentrations of copper in the sediments, and anthropogenic inputs from nearby sources (Cain and Luoma 1990). In cockles (*Cerastoderma edule*), copper concentrations in tissues decrease with increasing age, decrease in summer when compared to other seasons, and increase with increasing sediment copper concentrations (Savari et al. 1991). In the cockle (*Anadara trapezium*), tissue copper concentrations are positively related to dissolved copper concentrations in the water column and independent of sediment copper concentrations (Scanes 1993). Small freshwater clams (*Anodonta grandis*) have higher copper concentrations in soft tissues than large clams because small clams take up copper at a greater rate and excrete it more slowly than large clams (Pip 1990); a similar case is made for oysters and other bivalve mollusks (Weis et al. 1993a). Zebra mussels (*Dreissena polymorpha*) regulate body copper concentrations at water copper levels of 13 µg Cu/L and lower (Camusso et al. 1994). Proximity to point sources, such as sewage discharge plants, is associated with elevated copper burdens in common mussels, *Mytilus edulis* (Ward 1990). Copper concentrations increased in mussels (*Mytilus* spp.) analyzed in the coastal mussel watch program between the late 1970's and the late 1980's. This may be due to increased availability of copper from

anthropogenic sources; however, concentrations of other metals (silver, nickel, cadmium, lead, zinc) in mussels analyzed during this period showed a decrease (Lauenstein et al. 1990).

Pacific oysters near a copper recycling facility in Taiwan have elevated concentrations of copper (as high as 4,400 mg/kg DW soft parts), a characteristic green color, and low survival after exposure to waste effluents for 3 months (Hung et al. 1990). Diet is the major pathway by which greenish-colored Pacific oysters accumulate copper; initial daily accumulation rates are as high as 214 mg Cu/kg DW soft parts (Han and Hung 1990). Elimination of 50% of the copper from green Pacific oysters with elevated copper loadings takes only 11.6 days vs. 25.1 days in reference oysters (Han et al. 1993). Elevated concentrations of copper in Pacific oysters (135 mg/kg DW soft parts) near a marina in Arcachon Bay, France, are attributed to the ban on tributyltin antifouling paints in 1982 and the subsequent growing use of copper-based antifouling paints (Claisse and Alzieu 1993). Copper concentrations in soft tissues of the American oyster are higher in oysters from low salinity waters than those from more saline waters; accumulations are not related to sediment copper concentrations in the immediate environment (Huggett et al. 1975). In Maryland, copper concentrations in tissues of the American oyster are seasonally highest in July and lowest in October and higher in low salinity waters than in high salinity waters (Roesijadi 1994). In Australia, copper concentrations in oyster soft parts from the Georges River, New South Wales, rose from 20 mg/kg FW to 46 mg/kg FW in the 1970's to as high as 93 mg/kg FW in 1987, possibly as a result of urban and industrial discharges; this concentration exceeds the recommended limit of 70 mg Cu/kg FW in shellfish edible tissues for protection of human health in Australia (Brown and McPherson 1992).

In amphipod (*Orchestia gammarellus*) crustaceans, copper concentrations vary seasonally due to variable copper loadings, are higher in organisms from contaminated sites than reference sites, and higher in females with juveniles in the brood pouch than females without juveniles (Moore et al. 1991). The existence of copper-rich granules is common to all invertebrate phyla; these granules are usually found in the digestive gland or its evolutionary equivalent, and their formation is related to high concentrations of copper in the immediate environment (Weeks 1992). The tolerance of talitrid amphipods to high concentrations of ambient copper is attributable, in part, to the formation of intracellular granules within the cells of the ventral caeca (Weeks 1992). In the shore crab (*Carcinus mediterraneus*), tissue copper concentrations are lower in winter than in summer and correlate positively with total protein and hemolymph copper contents (Devescovi and Lucu 1995). Elevated copper burdens in hemolymph of crabs probably reflects the incorporation of copper atoms in the structure of hemocyanin, the major hemolymph protein (Depledge et al. 1993). Marine decapod crustaceans regulate tissue copper concentrations within the range of 25 to 35 mg/kg DW (Neff and Anderson 1977).

In *Limnodrilus* sp., an oligochaete worm, copper bioavailability from surficial freshwater sediments is associated with the amount of copper present in the manganese oxide fraction of the sediment. The redox potential and pH in the gut of *Limnodrilus* allows the dissolution of the manganese oxide coating, making copper and other metals available for uptake (Diks and Allen 1983).

Copper concentrations in freshwater fishes collected nationwide in the United States have not changed significantly since 1978 (Schmitt and Brumbaugh 1990). In 1984, samples with the highest copper concentrations were Mozambique tilapia *(Tilapia mossambica)* from Hawaii and white perch (*Morone americana*) from the Susquehanna River in Maryland. These locations have historically yielded fish with relatively high concentrations of copper; in Hawaii, this may develop from copper-containing pesticides (Schmitt and Brumbaugh 1990). Copper concentrations in fishes are usually higher in liver than other tissues, higher in fish from copper-contaminated lakes than reference lakes, and higher in small fish than large fish of the same species (Cuill et al. 1970; Eisler 1984; ATSDR 1990; de Wet et al. 1994; Table 3). Residue data on copper in fish that are dead on collection are probably worthless for purposes of risk assessment owing to copper accumulation after death (Eisler and Gardner 1973). Among sharks collected in British waters, copper concentrations in all tissues are highest from inshore demersal species and lowest from offshore pelagic species, with males having higher copper concentrations in liver than females (Vas 1991).

Copper concentrations in tissues of marine vertebrates tend to decrease with increasing age of the organism (Law et al. 1992). Concentrations of copper in marine and coastal vertebrates—including elasmobranchs, teleosts, and pinniped mammals—are related to the age of the animal. Regardless of species or tissues, except brain, concentrations decrease with increasing age of the organism; brain copper concentrations in marine mammals increase with organism age (Eisler 1984). Decreases in tissue copper content are also associated with spawning migrations of salmonids when entering freshwater from the sea and with reproductive cycles of cod and other gadoids (Eisler 1984). In the copper-contaminated Miramichi River, Canada, populations of Atlantic salmon (*Salmo salar*) are reduced in numbers due to poor survival and reproduction (Sprague et al. 1965). Copper-containing mine wastes entering the Northwest Miramichi River cause many adult Atlantic salmon on their normal upstream spawning migration to return prematurely downstream; about 62% do not reascend. Downstream returns of salmon rose from 1 to 3% before pollution to 10 to 22% during four years of pollution. During some periods, dissolved copper and zinc concentrations exceed the lethal levels for immature salmon

and the avoidance concentrations for subadults (Sprague et al. 1965; Saunders and Sprague 1967).

In polar bears, concentrations of copper in liver are 3-5 times higher than their seal diet (Braune et al. 1991). Copper concentrations in liver and kidney of polar bears are lower in juveniles than adults (Norheim et al. 1992), which is contrary to a reverse trend noted in most species of vertebrates. Neonatal marine mammals, for example, have higher concentrations of copper in liver than those found in the mother (Law et al. 1992). The use of copper herbicides in Florida to control aquatic plants may be hazardous to the endangered manatee. Copper concentrations in livers of these aquatic herbivores from areas of high copper herbicide use are as high as 1,200 mg/kg DW. The maximum copper concentrations in livers of copper-challenged manatees are higher than any copper concentration measured in any species of free-ranging mammalian wildlife and are comparable to copper concentrations in livers of some species of domestic animals poisoned by copper (O'Shea et al. 1984).

Amphibians and Reptiles

Eggs of the Jefferson salamander (*Ambystoma jeffersonianum*) from a series of ponds that contain 1-25 µg Cu/L have—at the higher copper concentrations—a reduction in hatching success and an increase in embryonic mortality (Horne and Dunson 1995).

For reasons unknown, livers of some adult giant toads (*Bufo marinus*) normally contain grossly elevated concentrations of copper (>2,000 mg/kg DW). The toads' livers are undamaged by this level of copper, and this lack of effect is in sharp contrast to human patients with Wilson's disease (2,000 mg Cu/kg DW liver) wherein hepatocyte degeneration, necrosis, and ultimately cirrhosis result (Goldfischer et al. 1970). In toad livers, the copper is sequestered in lysosomes, which seems to protect the cell from the toxic effects of copper. In contrast, copper in livers of humans with Wilson's disease is diffusely distributed in the cytoplasm of hepatocytes and is associated with severe and often fatal pathological changes (Goldfischer et al. 1970).

Birds

Season of collection and organism age affect copper concentrations in avian tissues. In livers of surf scoters (*Melanitta perspicillata*) from San Francisco Bay, copper concentrations are higher in March than in January; in livers of canvasbacks (*Aythya valisineria*) from Louisiana, concentrations are lower in November than later months; and in primary flight feathers of mallards (*Anas platyrhynchos*) and black ducks (*Anas rubripes*) from the vicinity of a smelter in Sudbury, Ontario, copper concentrations are highest in autumn (Ranta et al. 1978). Copper concentrations in tissues of coastal seabirds tend to decrease with increasing age (Eisler 1984). In New Zealand, younger marine birds have higher concentrations of copper in livers than adults (Lock et al. 1992). But juveniles and adults of common murres (*Uria aalge*) from Scotland have similar concentrations of copper in kidneys, livers, and muscle (Stewart et al. 1994).

In general, birds retain a very small portion of copper and other metals ingested (Bryan and Langston 1992). It is therefore noteworthy that livers of some canvasbacks collected in Louisiana (Custer and Hohman 1994) and livers of some mute swans (*Cygnus olor*) from England (Bryan and Langston 1992) both contain more than 2,000 mg Cu/kg DW. In the case of mute swans, several thousands of milligrams of copper per kilogram dry weight occur in the blackened livers; blackening is attributed to ingestion of flakes of copper-based antifouling paints (Bryan and Langston 1992). Tree swallows (*Tachycineta bicolor*) nesting near acidified aquatic ecosystems accumulate sufficient copper from the diet to induce elevated hepatic metallothionein concentrations (St. Louis et al. 1993). However, there is no evidence of copper biomagnification in the sediment food chain of sediment-pondweed-red-knobbed coot (*Fulica cristata*; van Eeden and Schoonbee 1993).

Mammals

Impalas (*Aepyceros melampus*) found dead in Kruger National Park, South Africa, had elevated concentrations of copper in livers (maximum 444 mg/kg FW) and kidneys (maximum 141 mg/kg FW); authors assert that copper poisoning is the most likely cause of death (Gummow et al. 1991), but this needs verification. Copper concentrations in bones, kidneys, and livers of white-tailed deer (*Odocoileus virginianus*) near a copper smelter and from distant sites are about the same; however, deer near the smelter have significantly elevated concentrations of cadmium in kidneys and livers, lead in bone, and zinc in kidneys (Storm et al. 1994).

Only a small portion (0.037%) of copper mining wastes discharged into riparian wetlands is bioavailable to resident rodents, as judged by measurements of copper in carcasses of mice and voles (Pascoe et al. 1994). Populations of brown-backed voles (*Clethrionomys rufocanus*) and other microtine rodents (*Microtus* spp., *Lemmus*) are low or absent in the vicinity of Russian copper-nickel smelters (Kataev et al. 1994). The reasons for this decline are unknown but may be due to a decrease in the abundance of important food plants (lichens, mosses, seed plants), and—as shown in preference studies—to an avoidance of plants from the contaminated area (Kataev et al. 1994). Bank voles (*Clethrionomys glareolus*) from areas of Poland subjected to various degrees of industrial contamination have copper concentrations in tissues comparable to those in animals from polluted sites in North America and the United Kingdom (Sawicka-Kapusta et al.

1990). Compared to animals from a reference site, muskrats (*Ondatra zibethicus*) from a site contaminated by copper and other chemicals have higher concentrations of copper in kidneys, and have smaller spleens, larger adrenals, less fat, and lower body weight (Halbrook et al. 1993).

In Poland near copper foundries, livers from cattle (*Bos* sp.) have higher copper concentrations (35-140 mg/kg FW) than cattle from agricultural regions (7-32 mg/kg FW); however, kidney copper concentrations are comparable for both regions (Falandysz 1993a). Cattle found dead in South Africa near a copper smelter have elevated levels of copper in liver (600 mg/kg FW; 1,078 mg/kg DW); airborne copper from the smelter is considered the most likely cause of death (Gummow et al. 1991). Sheep held for 150 days in a paddock near a heavily-traveled highway have significantly elevated copper concentrations in wool; these differences are not as pronounced in hair from horses (*Equus caballus*) and alpacas (*Lama pacos*) held under similar conditions (Ward and Savage 1994).

Interspecies differences in copper contents are considerable. Serum from domestic dogs (*Canis familiaris*) lacks the strong copper binding site available on the serum albumin molecule of humans and rats. Accordingly, copper concentrations in livers from dogs (82 mg/kg FW; 336 mg/kg DW) are normally about 12 times higher than those of human livers and 19 times higher than those of rat livers (Goresky et al. 1968).

Human foods that are particularly rich in copper (20-400 mg Cu/kg) include oysters, crustaceans, beef and lamb livers, nuts, dried legumes, dried vine and stone fruits, and cocoa (USEPA 1980). In humans, copper is present in every tissue analyzed (Schroeder et al. 1966). A 70-kg human male usually contains 70-120 mg of copper (USEPA 1980). The brain cortex usually contains 18% of the total copper, liver 15%, muscle 33%, and the remainder in other tissues—especially the iris and choroid of the eye. Brain gray matter (cortex) has significantly more copper than white matter (cerebellum); copper tends to increase with increasing age in both cortex and cerebellum. In newborns, liver and spleen contain about 50% of the total body burden of copper (USEPA 1980). Liver copper concentrations were usually elevated in people from areas with soft water (Schroeder et al. 1966). Elevated copper concentrations in human livers are also associated with hepatic disease, tuberculosis, hypertension, pneumonia, senile dementia, rheumatic heart disease, and certain types of cancer (Schroeder et al. 1966).

Copper Deficiency Effects

General

Adverse effects of copper deficiency are documentable in terrestrial plants and invertebrates, poultry, small laboratory animals, livestock—especially ruminants—and humans. Data are scarce or missing on copper deficiency effects in aquatic plants and animals and in avian and mammalian wildlife. Copper deficiency in sheep—the most sensitive ruminant mammal—is associated with depressed growth, bone disorders, depigmentation of hair or wool, abnormal wool growth, fetal death and resorption, depressed estrous, heart failure, cardiovascular defects, gastrointestinal disturbances, swayback, pathologic lesions, and degeneration of the motor tracts of the spinal cord (NAS 1977).

Terrestrial Plants and Invertebrates

Copper is an essential micronutrient of all higher plants studied, being a cofactor for the enzymes polyphenol oxidase, monophenol oxidase, laccase, and ascorbic acid oxidase (Schroeder et al. 1966). In copper-deficient soils, copper is strongly held on inorganic and organic exchange sites and in complexes with organic matter (Thornton 1979), causing reduced availability of copper to vegetation in these soils. Copper deficiency in terrestrial plants is usually associated with reduced growth, abnormally dark coloration in rootlets, and chlorotic leaves (Gupta 1979). In agricultural crops, copper deficiency occurs at less than 1.6 mg dissolved Cu/kg DW soil (Thornton 1979), and in sensitive plants at less than 2 to less than 5 mg total Cu/kg DW leaves (Gupta 1979). In fruit trees, copper deficiency is characterized by death of apical buds, formation of multiple buds, and yellowing (chlorosis) of the leaf margins (NAS 1977). Copper deficiency in alfalfa (*Medicago sativa*) and clover (*Trifolium* spp.) is associated with a faded green leaf color, growth inhibition, and withering (Gupta 1979). In grasses, copper deficiency is characterized by chlorosis, stunting, and necrosis and in cereals by pale color, reduced growth, and a reduction in the number of pollen grains (Gupta 1979).

Increased yields of various crops occur when copper salts are added to fertilizers at 300 to 800 mg Cu/m^3 (NAS 1977). In corn (*Zea mays*) and other vegetables, younger plants are more sensitive to copper deficiency than mature plants; in all cases, copper-deficient vegetables show chlorosis, reduced growth and reproduction, and low survival (Gupta 1979).

No evidence of copper deficiency exists in terrestrial species of invertebrates examined; however, relatively low concentrations of copper stimulated growth and reproduction. Reproduction in mites (*Platynothrus peltifer*) increases when fed diets containing 28 mg Cu/kg DW (vs. 13 mg/kg in controls) for 3 months (Denneman and van Straalen 1991). And juvenile earthworms (*Eisenia andrei*) show increased growth at 18 mg Cu/kg DW soil after 12 weeks (van Gestel et al. 1991).

Aquatic Organisms

No documented report of fatal copper deficiency is available for any species of aquatic organism. And no correlation is evident in aquatic biota for the presumed nutritional

copper requirements of a species and its sensitivity to dissolved copper (Neff and Anderson 1977). Extremely low copper concentrations (5.5 and 6.7 mg/kg DW) in whole bodies of 2 of 17 species of crustaceans from the Antarctic Ocean support the hypothesis that certain Antarctic species may show copper deficiencies or reduced metal requirements (Petri and Zauke 1993).

Birds and Mammals

Copper deficiency is not a major public health concern in the United States (Percival 1995). Copper deficiency is rarely observed in humans except in cases of severely malnourished children or those with Menkes' disease—an X-linked recessively inherited disorder. This disease is a severe congenital copper deficiency marked by slow growth, progressive cerebral degeneration, convulsions, temperature instability, bone alterations, and peculiar steel-like hair (ATSDR 1990; Yoshimura et al. 1995). Treatment of Menkes' disease is now restricted to parenteral administration of copper salts, although complete prevention of neurodegradation is difficult to obtain (Yoshimura et al. 1995). Copper deficiency is sometimes reported in humans after intestinal resection surgery (reduced absorptive surface), in people who consume high levels of zinc (zinc induces intestinal metallothionein that blocks copper transport), in infants who consume a diet based on cow milk (cow milk is a poor source of copper), and in genetic cases (Percival 1995). Moderate copper deficiency also exists in burn and trauma patients, two groups at high risk for sepsis (DiSilvestro et al. 1995).

An inherited abnormal copper metabolism has been established in certain strains of mice, rats, and dogs (Sugawara and Sugawara 1994). Feeding a copper-deficient diet to these animals may prevent acute hepatitis. In rats with abnormal copper metabolism and hereditary hepatitis, the feeding of a copper-deficient diet (0.5 mg Cu/kg ration for 35 days) prevents copper accumulation (94-139 mg Cu/kg DW liver) and dysfunction. But feeding a normal diet of 30 mg Cu/kg DW ration to these rats produces liver copper concentrations of 375 mg/kg DW (Sugawara and Sugawara 1994). Administered copper protects copper-deficient strains of mice against neurodegradation, and protects ponies against selenium poisoning when pretreated with 20 or 40 mg Cu/kg BW (Stowe 1980).

Chickens (*Gallus domesticus*) given diets deficient in copper (less than 2.7 mg kg ration) have anemia, poor growth, low survival, and a high frequency of cardiovascular and skeletal lesions (Carlton and Henderson 1963, 1964a, 1964b). It is emphasized, however, that copper deficiency does not usually arise from eating a copper-poor diet because copper is found ubiquitously in foods (Percival 1995). Chickens, turkeys (*Meleagris gallopavo*), cattle, and pigs deficient in copper are prone to die suddenly (Gallagher 1979). Sudden death in some copper-deficient species is sometimes associated with rupture of a major blood vessel or rupture of the heart (Carlton and Henderson 1964b; NAS 1977; ATSDR 1990; Saari et al. 1994). Male weanling rats given a copper-deficient diet of 0.13 mg Cu/kg ration (vs. copper-normal diet of 5.7 mg Cu/kg ration) for 7 weeks show high mortality (24%) from cardiac rupture; ruptured hearts had elevated concentrations of sodium, potassium, and calcium, and depressed magnesium (Saari et al. 1994). Copper deficiency in weanling rats is confirmed by low activities of ceruloplasmin in serum and by superoxide dismutase in liver and serum (DiSilvestro et al. 1995). Skeletal deformities and leg fractures occur in copper-deficient chickens, dogs, pigs, sheep, cattle, and children because of decreased tensile strength of bones (Carlton and Henderson 1964a; NAS 1977; Gallagher 1979). In lambs from copper-deficient ewes, locomotor disturbances of gait or posture occur because of lesions of excessive myelination of the central nervous system (Gallagher 1979).

Copper deficiency in humans and other mammals is characterized by slow growth, hair loss, anemia, weight loss, emaciation, edema, altered ratios of dietary copper to molybdenum and other metals, impaired immune response, decreased cytochrome oxidase activity, central nervous system histopathology, decreased phospholipid synthesis, fetal absorption, and eventually death (NAS 1977; Gallagher 1979; Kirchgessner et al. 1979; USEPA 1980; ATSDR 1990; Percival 1995).

In laboratory white rats, signs of copper deficiency include reductions in tissue copper concentrations; reduced activities of cytochrome oxidase, superoxide dismutase, succinoxidase, and ceruloplasmin; increased activity of 7-ethoxyresorufin *O* deethylase (EROD) in small intestines; anemia associated with low hematocrit and hemoglobin; increased acute inflammatory response; increased sensitivity to endotoxins; central nervous system lesions; and reduced phospholipid synthesis (Gallagher 1979; Johnson and Smith 1994; Schuschke et al. 1994; DiSilvestro et al. 1995). Copper-deficient rats also have prolonged sleeping times and significant reductions in activities of aniline hydroxylase and hexobarbital oxidase in liver (Moffitt and Murphy 1973). Earliest signs of copper deficiency in rats include low concentrations of copper in livers (1.4-<3.0 mg/kg DW vs. 12.6-15.0 mg/kg DW in controls); profound reductions in activities of cytochrome oxidase and succinoxidase; and reductions in hematocrit, hemoglobin, ceruloplasmin, and phospholipid synthesis (Gallagher 1979; Johnson and Smith 1994). Severe copper deficiency in rats results in anemia characteristic of defective hemoglobin synthesis resulting from abnormal use of iron by mitochondria in heme synthesis (Johnson and Smith 1994). Copper-deficient rats are extraordinarily sensitive to endotoxins and die after receiving normally sublethal doses of various endotoxins (DiSilvestro et al. 1995). Copper deficiency-induced lesions in the central nervous system are produced experimentally in rats and guinea pigs and are a characteristic feature of Menkes' disease (Gallagher 1979).

Sway disease of bactrian camels (*Camelus bactrianus*)—characterized by anemia, emaciation, falling, fractures, and death—is caused by copper deficiency associated with high molybdenum content in soils and forage; deficiency effects are aggravated during reproduction (Zong-Ping et al. 1994).

Sheep fed copper-deficient diets of less than 2.5 mg Cu/kg DW ration (vs. a normal diet of 11.0 mg Cu/kg DW) produce a high frequency of swaybacked lambs. Swaybacks have lower concentrations of copper in liver than nonswaybacked lambs from copper-deficient ewes; both groups have lower concentrations of copper in livers than normal lambs (Lewis et al. 1967; Buckley and Tait 1981).

Copper deficiency effects are reported in mink (*Mustela vison*) and domestic swine. Copper deficiency in mink, as judged by reduced survival, occurs by feeding rations containing the equivalent of 3.5 mg Cu/kg BW daily for a period of 50 weeks (ATSDR 1990). Swine, which seem to have higher copper requirements than mink, given low copper diets equivalent to 15 to 36 mg Cu/kg BW daily for 7 days have decreased hemoglobin, hematocrit, and growth rate (ATSDR 1990).

Dietary copper deficiency increases the acute inflammatory response in rats and other small laboratory animals (Schuschke et al. 1994). The release of inflammatory mediators, such as histamine and serotonin, from mast cells increases the vascular permeability of postcapillary venules and results in edema. In copper-deficient rats, release of histamine from mast cells positively correlates with frequency of the acute inflammatory response. Copper-deficient rats (0.6 mg Cu/kg DW ration for 4 weeks) have more mast cells in muscle than copper-adequate controls given diets containing 6.3 mg Cu/kg DW ration; however, histamine content of mast cells is not affected (Schuschke et al. 1994). An early clinical sign of copper deficiency is a reduction in the number of circulating neutrophils; the mechanism for copper-deficient neutropenia (leukopenia in which the decrease in white blood cells is chiefly neutrophils) is unknown (Percival 1995). Proposed mechanisms to account for neutropenia from copper deficiency include (1) early destruction of bone marrow progenitor cells; (2) impaired synthesis of neutrophils from progenitor cells; (3) a decrease in the rate of cellular maturation in the bone marrow; (4) impaired secretion of neutrophils from the bone marrow; and (5) rapid clearance of circulating copper-deficient neutrophils (Percival 1995).

Lethal and Sublethal Effects

General

Copper is toxic to sensitive species of terrestrial vegetation at greater than 40 µg/L nutrient solution (seedlings of pines, *Pinus* spp.), at greater than 10 mg/kg DW leaves (cucumber, *Cucumis sativus*), and greater than 60 mg extractable Cu/kg DW soil (sweet orange, *Citrus sinensis*; Table 4). Among sensitive species of terrestrial invertebrates, adverse effects on survival, growth, or reproduction occur at 2 µg Cu/cm² on paper discs (earthworms), greater than 50 mg Cu/kg diet (larvae of gypsy moth, *Lymantria dispar*), and 53 to 70 mg Cu/kg DW soil (earthworms and soil nematodes; Table 4).

Table 4. Effects of copper on representative terrestrial plants and invertebrates.

Organism, copper concentration or dose, and other variables	Effects	Reference[a]
Plants		
Agricultural crops from soils containing dissolved copper		
0.0-1.6 mg/kg soil	Copper deficiency in susceptible crops	1
1.7-2.4 mg/kg soil	Slight deficiency	1
2.5-4.0 mg/kg soil	Deficiency unlikely	1
>4.0 mg/kg soil	Soil well supplied with copper	1
Sweet orange, *Citrus sinensis*; 4-year old trees; M3 extractable soil copper >60 mg/kg DW (from treated plots containing about 120 kg Cu/ha)	Growth adversely affected; positive correlation between copper concentrations in feeder roots (4 to 450 mg Cu/kg DW) and M3 extractable soil copper	17
Cucumber, *Cucumis sativus*; leaves		
<2 mg/kg dry weight (DW)	Deficient	2
2-10 mg/kg DW	Sufficient	2
>10 mg/kg DW	Toxic	2
Soybean, *Glycine max*; leaves		

Table 4. *Continued.*

Organism, copper concentration or dose, and other variables	Effects	Reference[a]
<4 mg/kg DW	Deficient	2
10-30 mg/kg DW	Sufficient	2
>50 mg/kg DW	Toxic	2
Pasture grasses; aboveground portions		
<5 mg/kg DW	Deficient	2
5-12 mg/kg DW	Sufficient	2
>12 mg/kg DW	Toxic	2
Seedlings of stone pine, *Pinus pinea* and maritime pine, *Pinus pinaster*; exposed to nutrient solutions containing 0.4 (controls) 4, 40, or 200 µg Cu/L for as long as 4 weeks		
4 µg/L	Slight to no enhancement of root elongation	16
40 µg/L	Taproot elongation reduced but partial growth recovery in 7 days; cell membrane damage evident after 10 days	16
200 µg/L	Root growth completely inhibited within 3 days in both species	16
Faba bean, *Vicia faba*; cultured hydroponically with nutrient solutions containing 100 mg Cu/L for 24 days; shoots analyzed before (day 4) and after (day 24) 20-day infestation by the black bean aphid, *Aphis fabae*. Controls were raised in copper-free nutrient solutions	Aphid infestation caused a significant reduction in copper content of shoots from 51 mg/kg DW to 17 mg/kg; copper in control was 25 mg/kg DW prior to aphid infestation and 14 mg/kg after 20-day infestation	3
Invertebrates		
Soil nematode, *Caenorhabditis elegans*		
70 mg/kg DW sandy soil for 24 h	LC50	4
105 mg/L for 24 h; no soil	LC50	4
1,061 mg/kg loam substrate for 24 h	LC50	4
2,476 mg/L for 24 h; loam substrate	LC50	4
Soil ciliate, *Colpoda steini*		
250 µg/L for 24 h	Growth reduced 50%	5
Fruitfly, *Drosophila melanogaster*		
In culture medium containing 80 µg cm^2 for 4 weeks	Survival reduced 35%; copper elevated in cytoplasm, malpighian tubule epithelial cells, and other tissues	6
Earthworms, three species; 40-238 mg/kg soil; exposure duration unknown	No effect on growth, survival, or reproduction	7
Earthworm, *Eisenia andrei*; juveniles; exposure for 12 weeks		
18 mg/kg DW soil	Growth stimulated	8
56 mg/kg DW soil	No effect on growth or reproduction	8
100 mg/kg DW soil	<50% effective in reducing growth; inhibited sexual development	8
Earthworm, *Eisenia fetida*		
32 mg/kg DW soil for 56 days	No effect on cocoon production	9
53.3 (32.5-186.0) mg/kg DW soil for 56 days	Cocoon production reduced 50%	9
210 mg/kg DW soil for 56 days	No deaths	9
555 (460-678) mg/kg DW soil for 56 days	50% dead	9
683 (570-812) mg/kg DW soil for 14 days	50% dead	9
Earthworm, *Eisenia fetida andrei*		
Adults held in soil containing as much as 300 mg/kg DW for 3 weeks; resultant	No adverse effects on cocoon production or hatchability in soil containing 60-120 mg/kg DW; adult growth	10

Table 4. *Continued.*

Organism, copper concentration or dose, and other variables	Effects	Reference[a]
cocoons incubated in uncontaminated soil for 5 weeks to assess hatchability	retarded during exposure at 300 mg/kg DW	
Earthworm, *Lumbricus rubellus*		
100-150 mg/kg DW soil	Decreased cocoon production	11
150-300 mg/kg DW soil	Decrease in litter breakdown activity	11
>300 mg/kg DW soil	Reduced growth and increased mortality	11
1,000 mg/kg DW soil for 6 weeks	Lethal to 50%	11
Earthworm, *Lumbricus terrestris*		
Exposed for five days to filter paper disc containing 0.5, 1, 2, 4, or 8 µg Cu/cm^2	At 4 µg/cm^2 and higher, mortality was >90%; 20% were dead at 2 µg/cm^2 and none were dead at lower concentrations. Whole worms contained, in mg Cu/kg DW, 5.9 in controls, 28.5 in the 0.5 group, and 73.1 in the 1.0 group. At sublethal concentrations, worms had decreased lysozyme activity in coelomic fluid and coelomocytes	12
Gypsy moth, *Lymantria dispar*		
Larvae were fed diets containing 10, 50, 250, or 1,250 mg/kg ration from first instar to pupation; effects measured on development rate, growth, survival, and reproductive success	No adverse effects at 10 mg/kg diet. Significant adverse effects at 50 mg/kg and higher on development and reproductive success and at 250 mg/kg and higher on growth	13
Oribatid mite, *Platynothrus peltifer*		
Fed diets with 13 (control), 28, 64, 168, 598, or 1,498 mg Cu/kg DW diet for 3 months	No deaths at any dose. Reproduction increased at 28 mg/kg but decreased steadily with increasing dose. The no-observable-effect-concentration (NOEC) for reproduction was 168 mg/kg diet; the NOEC for growth was 598 mg/kg. Copper concentrations in whole mites increased significantly at dietary loadings >168 mg/kg	7
84 mg/kg DW soil	NOEC on growth, survival, or reproduction	7
Soil faunal communities		
Forest soil treated to contain 100, 200, 400, or 600 mg Cu/kg DW; nematodes and macroarthropods enumerated after 7 days	Sensitive species of nematodes and mites were reduced in number at 100 mg/kg soil; total nematode and arthropod numbers declined at 200 mg/kg and higher	14
Termites, subterranean; Karachi, Pakistan; termite-infested area (*Microtermes* spp., *Heterotermes* spp., *Coptotermes* spp., *Odontotermes* spp.)		
Fir (*Abies pindrow*) wooden stakes coated with 5% copper sulfate in gelatin solution vs. uncoated stakes	Copper-treated stakes prevented termite attack in soil up to 4 years vs. severe termite damage within 6 months in control stakes	15

[a]1, Thornton 1979; 2, Gupta 1979; 3, Crawford et al. 1990; 4, Donkin and Dusenbery 1993; 5, Forge et al. 1993; 6, Marchal-Segault et al. 1991; 7, Denneman and van Straalen 1991; 8, van Gestel et al. 1991; 9, Spurgeon et al. 1994; 10, van Gestel et al. 1989; 11, Ma 1984; 12, Goven et al. 1994; 13, Gintenreiter et al. 1993; 14, Parmelee et al. 1993; 15, Roomi et al. 1990; 16, Arduini et al. 1995; 17, Alva et al. 1995.

Sensitive species of representative freshwater plants and animals die within 96 h at waterborne copper concentrations of 5.0 to 9.8 µg/L (Hodson et al. 1979; Table 5). The most sensitive freshwater species have LC50(96 h) values between 0.23 and 0.91 µg Cu/L and include daphnids (*Daphnia* spp.), amphipods (*Gammarus pseudolimnaeus*), snails (*Physa* spp.), and chinook salmon (*Oncorhynchus tshawytscha*; USEPA 1980; Table 5). In general, mortality of tested aquatic species is greatest under conditions of low water hardness (as measured by $CaCO_3$), starvation, elevated water temperatures, and among early developmental stages (Hodson et al. 1979; Table 5). Toxicity testing of copper-contaminated sediments to amphipods (*Hyalella azteca*) and daphnids (*Daphnia magna*) using techniques of enzyme inhibition and growth rate show that these variables are more sensitive in accurately predicting

copper sensitivity than LC50 (48 h) values (Kubitz et al. 1995) and should be considered when assessing risk of contaminated sediments to freshwater systems. The most sensitive saltwater species to copper have LC50 (96 h) values from 28 to 39 µg/L and include summer flounders (*Paralichthys dentatus*), copepods (*Acartia tonsa*), and softshell clams (*Mya arenaria*; USEPA 1980; Eisler 1995; Table 5). Adverse sublethal effects of copper on representative species of estuarine algae, mollusks, and arthropods frequently occur at 1 to 10 µg/L (Bryan and Langston 1992; Table 5).

No data are available on copper toxicity to avian wildlife. Experiments with domestic poultry show that copper accumulates in livers of mallard ducklings at dietary concentrations as low as 15 mg/kg DW ration; that gizzard histopathology and a reduction in weight gain of chicks (*Gallus* sp.) occur at 250 to 350 mg Cu/kg DW ration; and that growth of turkey poults is improved at 60 mg Cu/kg DW ration and inhibited at 120 mg/kg DW ration, with signs of gizzard histopathology at 500 mg/kg DW ration (Wood and Worden 1973; Poupoulis and Jensen 1976; NAS 1977; Kashani et al. 1986; Table 6).

Table 5. Effects of copper on representative aquatic plants and animals.

Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
Plants		
Algae; mixed culture; 5 µg/L	Photosynthesis reduced	1
Aquatic weeds, fresh water		
170 µg/L for 99 days, continuous exposure	Eliminated or controlled most submerged species; adverse effects first noted at day 34. Weeds contained 360 to 4,280 mg/kg dry weight (DW)	2
250-1,000 µg/L for 99 days, continuous exposure	Unsuccessful in controlling emergent aquatic weeds; successful in eliminating filamentous algae and most submerged species	2
Marine alga, *Chlamydomonas bullosa*; 49.9 µg/L for 96 h	Growth reduced 50%	3
Green alga (fresh water), *Chlamydomonas reinhardtii*		
18 µg/L for 24 h	Reduction in number of cells bearing flagella	4
21 µg/L for 7 days	Growth normal	5
32 µg/L for 7 days	Growth reduced 50%	5
60 µg/L for 10 min	Flagella shed; flagellar refabrication inhibited for 24 h	4
79 µg/L for 72 h	Growth inhibited 50%	5
Freshwater alga, *Chlorella* spp.		
1.0 µg/L	Growth reduced	1
6.3 µg/L	Photosynthesis inhibited	1
Marine alga, *Dunaliella salina*		
0.031 µg/L for 8 months	Minor adverse effects on lipid metabolism	6
380 µg/L for 96 h	Growth reduced 50%; negligible effects on cellular ultrastructure	3, 6
Marine alga, *Dunaliella tertiolecta*		
8,000 µg/L for 48 h	Growth normal	7
12,000-16,000 µg/L for 48 h	Adverse effects on photosynthesis, cell division rates, and pigment metabolism	7
Euglena, *Euglena gracilis*; 10,000 µg/L for 5 days	Adverse sublethal effects, including altered free cysteine metabolism	8
Freshwater diatom, *Nitzschia palea*; 5 µg/L	Complete inhibition of growth	1
Alga, *Ochromonas danica*		
10,000 µg/L for as long as 9 days	Growth normal	11
Aquatic moss, *Rhynchostegium riparioides*; 4.5 (controls), 9, 21, or 50 µg/L for 27 days followed by 14 days in clean media	Copper accumulation plateaued after 18 days. Maximum concentrations reached, in mg/kg DW, were 900 (9 µg/L group), 2,000 (20 µg/L group), and 3,500 (50 µg/L group).	12

Table 5. *Continued.*

Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
	At end of depuration mosses had lost about 50% of accumulated copper	
Freshwater alga, *Scenedesmus acutiformis*; 100 µg/L for 20 min at pH 4.8, 5.8, or 6.8	Copper concentrations, in mg/kg DW, increased from 400 (pH 4.8) to 750 (pH 5.8) to 4,000 (pH 6.8)	10
Freshwater alga, *Scenedesmus subspicatus*		
56 µg/L for 72 h	Growth normal	5
120 µg/L for 72 h	Growth reduced 50%	5
Marine alga, *Scrippsiella faeroense*; 5 µg/L for 5 days	Growth inhibited 50%	1
Marine alga, *Thalassiosira pseudonana*; 5 µg/L for 72 h	Growth inhibited 50%	1
Protists		
Freshwater protozoan ciliate, *Tetrahymena pyriformis*		
3,818 µg/L for 96 h	Growth normal	5
8,000 µg/L for 48 h	Growth inhibited 50%	5
Cnidarians		
Sea anemone, *Anemonia viridis*; 50 or 200 µg/L for 5 days	Immediate tentacle retraction; copious production of mucus; progressive visible bleaching and loss of zooxanthellae	13
Hydroid, *Campanularia flexuosa*		
1.4 µg/L for 11 days	Enzyme disruption	1
10-13 µg/L for 11 days	Growth rate reduced	1
Ctenophore, *Pleurobrachia pileus*; 33 µg/L for 24 h	Fatal to 50%	1
Rotifers		
Freshwater rotifer, *Brachionus calyciflorus*		
2.5-5.0 µg/L	MATC[b]	14
14 µg/L for 5 h	Swimming behavior impaired 50%	14
25 µg/L for 5 h	All immobilized	14
26 µg/L for 24 h	Fatal to 50%	14, 15
34 µg/L for 5 h	Feeding rate reduced 50%	15
43 µg/L for 24 h	Feeding rate reduced 50%	16
80 µg/L for 24 h	No deaths when molar ratio of fulvic acid to copper was 1:1	17
Nematodes		
Free-living nematode, *Caenorhabditis elegans*		
260 µg/L for 96 h	LC50	18
22,000 µg/L for 24 h	LC50	18
Mollusks		
Freshwater unionid mussel, *Anodonta cygnea*		
2.1 (95% confidence interval [= CI] of 0.01-7.2) µg/L for 72 h	Reduction by 50% in valve closure of glochidia; ability to infect fish reduced	19
5.3 µg/L for 48 h	Valve closure rate reduced 50%	19
Freshwater mussel, *Anodonta grandis*		
17 µg/L for 24 h	Valve closure normal	20
33 µg/L for 24 h	Valve closure rate reduced 50%	20
44 µg/L for 24 h	Fatal to 50%	20
Bay scallop, *Argopecten irradians*		
5.0 µg/L for 119 days	All dead	1

Table 5. *Continued.*

Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
5.8 µg/L for 42 days	Growth rate reduced 50%	1
Freshwater snail, *Biomphalaria glabrata*; 60 µg/L for 60 h	Lethal; epithelial cell histopathology	21
Freshwater snail, *Bulinus globosus*; 707 µg/L for 24 h	LC50	22
Channeled whelk, *Busycon canaliculatum*		
100 µg/L for 54 days	Copper concentrations, in mg/kg FW, were 43 (vs. 35 in controls) in gills and 25 (vs. 16) in osphradium	23
500 µg/L for 16 days	All dead	23
Snail, *Campeloma decisum*		
>30 µg/L for 24 h	Motility inhibited	24
1,700 µg/L for 96 h	LC50	24
Asiatic clam, *Corbicula fluminea*		
5.5 µg/L for 30 days	Growth normal; soft tissues contained 80 mg/kg DW (vs. 40-60 in controls)	25
8.4-26.7 µg/L for 30 days	Some deaths; growth reduction in juveniles and adults; soft parts had 205-278 mg/kg DW	25
19.2 µg/L for 30 days	LC50	25
Pacific oyster, *Crassostrea gigas*		
Adults		
10 µg/L for 14 days	LC20	27
100 µg/L	No deaths in 96 h; 30% dead in 14 days	27
560 µg/L for 96 h	LC50	27
Embryos, exposed for 48 h		
5 µg/L	94-98% normal development vs. 97-99% in controls	28
6.5 µg/L	8-25% abnormal (retarded shell size, reduced growth, erratic swimming behavior)	28
10 µg/L	26-79% abnormal	28
18 µg/L	No embryos developed normally	28
American oyster, *Crassostrea virginica*; adults with soft parts containing 837 mg/kg DW were held in flowing seawater of 1-2 µg Cu/L for 56 weeks	No significant depuration; soft parts contained 746-1,526 mg/kg DW during exposure	26
Clam, *Donax incarnatus*		
4.0 µg/L for 4 h	Increased oxygen consumption and increased ammonia excretion	29
26.1 µg/L for 96 h	LC50	29
Zebra mussel, *Dreissena polymorpha*		
4.5, 9, 21, or 50 µg/L for 27 days followed by 14 days in clean media	No deaths. Filtration rate reduced in 50 µg/L group during exposure but not afterwards. Maximum concentrations, in mg/kg DW soft parts, were about 30 (9 µg/L), 70 (21 µg/L), and 100 (50 µg/L); about 18% of the accumulated copper was lost during depuration	12
13 µg/L for 9 weeks	No effect on survival or filtration rate	30
>28 µg/L for 48 h	Copper accumulation	31
41-43 µg/L for 48 h to as long as 9 weeks	Filtration rate reduced 50%	30, 31
90 µg/L for 9 weeks	28% dead; 78% reduction in filtration rate	30
Black abalone, *Haliotis cracherodii*; 50 µg/L for 96 h	LC50	1
Red abalone, *Haliotis rufescens*; 86 µg/L for 96 h	LC50	1

Table 5. *Continued.*

Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
Freshwater mussel, *Lamellidens marginalis*		
250 µg/L for 96 h	Moribund; complete dissolution of crystalline style in 9.8 h; style reforms in 2.5 h on transfer to uncontaminated media and this may be useful as indicator of copper stress	32
250, 500, 750, or 1,000 µg/L for 30 days	No deaths. Initial dose-dependent increase in respiratory rate and decrease in growth rate; similar to controls by day 30	33
5,000 µg/L for 96 h	LC50	32, 33
Baltic clam, *Macoma balthica*; 40 µg/L for 48 h	Copper in soft parts was 23.5 mg/kg DW vs. 20.0 in controls	34
Clam, *Macoma liliana*; juveniles held in sediments containing <1 (controls), 5, 10, 15, 25, 30, 50, 70, or 140 mg/kg DW.	Maximal avoidance was in sediments containing 25 mg/kg and higher (interstitial water had 113 µg/L). Ability to bury in sediments was inhibited in sediments	35
Effects on avoidance in 96 h, burial rate in 90 min, and survival in 10 days were measured	Containing 15 mg/kg and higher (pore water of 120 µg/L). Reduced survival at 30 mg/kg DW sediment and higher	
Quahaug clam, *Mercenaria mercenaria*		
25 µg/L for 77 days	53% dead	1
640-6,400 µg/L	Dose-dependent increase in cytotoxicity by isolated brown cells	36
Scallop, *Mizuhopecten yessoensis*; 25 µg/L for 21 days	Hepatopancreas had 513 mg/kg DW (vs. <50 in controls); accumulations accompanied by a significant increase in hydroperoxide and malondialdehyde contents in microsomal membranes and alterations in lipid peroxidation rates	37
Softshell clam, *Mya arenaria*		
35 µg/L for 168 h	LC50 at 22° C	38, 160
39 µg/L for 96 h	LC50	1
86 µg/L for 504 h	LC50 at 17.5° C	38, 160
3,000 µg/L for 336 h	No deaths at 4° C	38, 160
Common mussel, *Mytilus edulis*		
0, 1, 3.2, 10, 32, or 100 µg/L for 7 days; mantle tissue analyzed for heat shock protein 60	Adverse effects on growth in the 32 and 100 µg/L groups; dose-dependent protein increase at 3.2 µg/L and higher	39
Mussels age 2.5 months continuously exposed to 0, 1, 5, or 10 µg/L for 21 months. Growth, histopathology, and residues in soft parts measured after 12, 18, and 21 months	Growth adversely affected in the 10 µg/L group; histopathology evident in the 5 and 10 µg/L groups. After 21 months, concentrations in soft parts, in mg/kg FW, were 5.5 in controls and the 1.0 µg/L group, 19.2 in the 5 µg/L group, and 62 in the highest exposure group	40
1, 3.2, 10, 32, or 100 µg/L for 7 days	No effect on protein activity in gill and mantle at 32 µg/L and lower; increased accumulations at 100 µg/L. At 32 µg/L and higher growth was reduced. At 100 µg/L survival decreased and copper concentrations increased from 24 to 89 mg/kg DW in gill and from 14 to 54 mg/kg DW in mantle	41
2 µg/L for 30 days	Spawning frequency reduced 50%	42
5-6 µg/L for 10 days	Growth reduced 50%	42
50 µg/L for 6 days, then transferred to clean seawater	Lysosomal destabilization in all age groups; ability to recover declined with increasing age	43
430 µg/L for 120 h	Cardiac activity reduced 50% within 4 h and reduction persisted for 120 h	44
Dipped for 5 sec in $CuSO_4$ solutions containing 5, 10, 25, or 50 g/L and stored	Fatal at 5 to 10 g/L if kept out of water for 24 h; fatal at 10-20 g/L if stored only a few hours. Oysters (*C. virginica*)	45

Table 5. *Continued.*

Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
in air for 6, 24, or 48 h	survived this treatment	
Mussel, *Mytilus galloprovincialis*		
15 µg/L for 5 days	Stimulates the synthesis of thionein-like copper-binding proteins in gill, mantle, and digestive gland	46
40 µg/L for 6 days	Gills contained 22.3 mg/kg FW (vs. 2.4 in controls); digestive gland had 6.8 mg/kg FW (3.0). Exposed mussels show stimulated lipid peroxidation rates in tissues	47
80 µg/L for 2 h	Induces the synthesis of copper-binding proteins similar to that of metallothioneins in gills and mantle	46
Common Limpet, *Patella vulgata*; 10 µg/L for 6 h	Pedal mucus production reduced 40%	48
Brown mussel, *Perna indica*		
2-6 µg/L for 4 h	Increased oxygen consumption	29
21.8 µg/L for 96 h	LC50	29
Green mussel, *Perna viridis*		
25 µg/L for 2 weeks	Reduction in filtration rate, growth, and oxygen to nitrogen ratio; histopathology of digestive cells and tissues. Residues, in mg/kg FW, were 38.2 in digestive gland vs. 2.6 in controls and 24.7 in total soft parts vs. 1.3 in controls	49
86 µg/L for 96 h	LC50	49
Snail, *Physa integra*		
15 µg/L for 6 weeks	No adverse effects on growth, survival, or feeding	24
39 µg/L for 96 h	LC50	1, 24
Apple snail, *Pomacea paludosa*; 24-57 µg/L for 96 h	LC50	50
Cuttlefish, *Sepia officinalis*; eggs; 4 (control), 50, 100, or 200 µg/L for 8 weeks	Dose-dependent decrease in hatching time and survival; no external malformations	51
Freshwater snail, *Thiara tuberculata*		
450 µg/L for 20 days	Progressive decline over time in oxygen consumption	52
2,180 µg/L for 72 h	LC50; survivors had decreased oxygen consumption	52
Giant clam, *Tridacna derasa*; embryos age 1 h; exposed at 27° C		
0.1 µg/L for 72 h	LC50	53
1.0 µg/L for 72 h	LC65	53
10.0 µg/L for 72 h	LC91	53
Clam, *Villorita cyprinoides*		
450 µg/L for 120 h	No deaths	54
1,000, 3,000, or 5,000 µg/L for 120 h	No deaths. Hemolymph protein levels reduced at 1,000 and 3,000 µg/L, but not in 5,000 µg/L	54, 161
Freshwater mussel, *Villosa iris*		
24 µg/L for 24 h	Valve closure normal	55
27-29 µg/L for 24 h	50% reduction in valve closure	55
83 µg/L for 24 h	LC50	55
Crustaceans		
Copepod, *Acartia clausi*; 52 µg/L for 96 h	LC50	1
Copepod, *Acartia tonsa*; 31 µg/L for 96 h	LC50	1
Amphipod, *Allorchestes compressa*		
3.7 µg/L for 4 weeks	Extrapolated concentration causing detectable decreases in survival and biomass	9

Table 5. *Continued.*

Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
10 µg/L for 4 weeks	Lowest concentration tested causing adverse effects on growth and survival; bioconcentration factor (BCF) of 51,500	9
500 µg/L for 96 h	LC50	9
Cladoceran, *Bosmina longirostris*		
1.4 µg/L for 48 h; starved	50% immobilized	56
3.7 µg/L for 48 h; fed	50% immobilized	56
16 µg/L for 15 days	Growth rate reduced	158
18 µg/L for 15 days	Survival reduced	158
Lesser blue crab, *Callinectes similis*		
50 µg/L for 118 days	No effect on survival or molting during exposure	57
250 µg/L; juveniles	LC50 (30 days); LC100 (68 days)	57
500 µg/L	50% of megalops dead in 3.7 days; 50% of juveniles dead in 7.7 days; all juveniles dead in 49 days	57
Crayfish, *Cambarus bartoni*; copper-tolerant strain exposed to 19 (controls), 125, 250, or 500 µg/L for 4 weeks; concentrations in controls (mg/kg DW) vs. all experimental groups (mg/kg DW)		
Exoskeleton	54 DW vs. 78-116 DW	58
Gills	368 DW vs. 571-1,167 DW	58
Hepatopancreas	1,778 DW vs. 1,494-2,346 DW	58
Muscle	88 DW vs. 99-129 DW	58
Viscera	92 DW vs. 158-276 DW	58
Shore crab, *Carcinus maenas*		
500 µg/L for 5-18 days	Gill histopathology; some recovery after exposure	59
500 µg/L for 28 days		
Controls (fed) vs. exposed (fed); values in mg/kg DW		
Carapace	5 DW vs. 51 DW	60
Midgut gland	26 DW vs. 474 DW	60
Controls (starved) vs. exposed (starved); values in mg/kg DW		
Carapace	4 DW vs. 72 DW	60
Midgut gland	298 DW vs. 583 DW	60
2,000 µg/L for 5 days	Some deaths; severe gill cellular hyperplasia	59
Daphnid, *Ceriodaphnia dubia*		
9.5 µg/L for 48 h	LC50 at pH 6.0-6.5	61
28 µg/L for 48 h	LC50 at pH 7.0-7.5	61
200 µg/L for 48 h	LC50 at pH 8.0-8.5	61
Cladoceran, *Chydorus sphaericus*		
3.3 µg/L for 48 h; starved	50% immobilized	56
7.6 µg/L for 48 h; fed	50% immobilized	56
Amphipod, *Corophium volutator*; exposed to <0.1, 50, or 100 µg/L for 14 days in seawater under conditions of normoxia, moderate hypoxia (29% oxygen saturation), and hypoxia (19% oxygen saturation)	Exposure to increasing levels of copper resulted in a significant increase in total body copper concentrations (from 76 to 174 mg/kg DW), and a lowering of egg production; mortality was higher at low oxygen saturations and high copper concentrations (max. 35% dead at 100 µg/L and 19% saturation)	62
Brown shrimp, *Crangon crangon*; 330	LC50	1

Table 5. *Continued.*

Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
µg/L for 96 h		
Daphnids, *Daphnia ambigua*, *D. parvula*, *D. pulex*; 49 µg/L for lifetime exposure	Reduced productivity	1
Daphnid, *Daphnia carinata*; 28 µg/L for 96 h	LC50	63
Daphnid, *Daphnia magna*		
5.9 µg/L for 21 days	Growth reduced 10%; bioconcentration factor (BCF) of 4,900; maximum whole body concentration of 43 mg/kg DW	64
10 µg/L for 96 h	LC50 at 45 mg $CaCO_3$/L	1
10 µg/L, life cycle	Inhibited reproduction	1
11.4-16.3 µg/L	MATC[b] at 51 mg $CaCO_3$/L	1
16.1 µg/L for 21 days	Growth reduced 50%	64
20-43 µg/L	MATC[b] at 104 mg $CaCO_3$/L	1
26-59 µg/L for 48 h; fed	LC50; no weight loss among survivors	65
28-58 µg/L for 48 h; starved	LC50; survivors had significant weight loss	65
59 µg/L for 26 h	Feeding rate reduced 50%	16
69 (37-110) µg/L for 21 days	LC50	64
200 µg/L for 96 h	LC50 at 226 mg $CaCO_3$/L	1
Daphnid, *Daphnia pulex*		
0.003-0.3 µg/L for 21 days	Increased reproduction	66
3 µg/L for 21 days	Impaired reproduction	66
5 µg/L for 70 days	Decreased survival beginning at day 58; no effect on reproduction	67
20-37 µg/L for 48 h	LC50	66, 67, 68
20 µg/L for 6 h daily for 70 days	Decreased survival and brood size	67
30 µg/L for 15 days	No significant effect on growth or survival	158
Daphnid, *Daphnia pulicaria*		
7.2-11.4 µg/L for 96 h	LC50 at 44-48 mg $CaCO_3$/L	1
17.8-27.3 µg/L for 96 h	LC50 at 95-245 mg $CaCO_3$/L	1
Amphipod, *Gammarus pseudolimnaeus*		
<4.6 µg/L for 15 weeks (two generations)	No adverse effects	24
4.6-8 µg/L	MATC[b] at 45 mg $CaCO_3$/L	1
6.2-12.9 µg/L for 5 weeks	Decreased survival	24
20 µg/L for 96 h	LC50	24
Amphipod, *Gammarus pulex*		
Immersed in solutions containing 2.6 (controls), 11, 14.6, 18.2 or 23.1 µg/L for 100 days	Population density doubled in the controls and the 11 µg/L group. Rate of increase was adversely affected at 14.6 and 18.2 µg/L; the high-dose group lost population. Low-dose groups were composed mainly of juveniles; at 14.6 µg/L and higher, the number of juveniles decreased; and at 18.2 µg/L and higher, number of adults decreased	69
33 µg/L for 240 h	LC50	69
Mysid shrimp, *Holmesimysis costata*; 17 µg/L for 96 h	LC50	70
American lobster, *Homarus americanus*		
48 µg/L for 96 h	Larval LC50	1
100 µg/L for 96 h	Adult LC50	1
Amphipod, *Hyalella azteca*		
1.3 (control), 5.6, 10, 18, 32, 56, or 100 µg/L	Survival reduced at 32 µg/L and higher; no significant	71

Table 5. *Continued.*

Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
for 10 weeks beginning at age 1-week	copper accumulations over controls in all groups	
1.3 (control), 5.6, 10, 18, 32, 56, 100, or 180 µg/L for 4 weeks; adults	Copper residues, in mg/kg DW, were 98 in controls; 122-150 for the 5.6-32 µg/L groups, and >196 for the high dose groups	71
17 µg/L for 96 h	LC50 at pH 6.0-6.5, adults	61
31 (28-35) µg/L for 10 days	LC50, juveniles	73
34 µg/L for 96 h	LC50; age 6-8 days	72
52 µg/L for 96 h	LC50; age 20-24 days	72
87 µg/L for 96 h	LC50 at pH 8.0-8.5	61
Freshwater prawn, *Macrobrachium rosenbergii*; 12 µg/L for 96 h	LC50	74
Freshwater prawn, *Macrobrachium rude*; 18-65 µg/L for 96 h	LC50-LC84	63, 75
Macroinvertebrate communities; 11.3 µg/L for 10 days	Abundance was reduced by 75% in laboratory studies vs. 44% in field experimental streams; number of taxa was reduced 56% in the laboratory vs. 10% in field streams	76
Peneid Shrimp, *Metapenaeus ensis*		
160 µg/L for 48 h	LC50 for larvae	77
250 µg/L for 2 h	Feeding inhibited >50%	77
4,760 µg/L for 48 h	LC50 for postlarvae	77
Cladoceran, *Moina irrasa*		
1.4 µg/L for 24 h	LC50 at pH 5.0, 30° C	78
2.8 µg/L for 24 h	LC50 at pH 6.5, 30° C	78
3.3 µg/L for 96 h	LC50 at pH 5.0, 20° C	78
5.5 µg/L for 48 h	LC50 at pH 5.0, 25° C	78
6.5 µg/L for 96 h	LC50 at pH 6.5, 20° C	78
7.5 µg/L for 96 h	LC50 at pH 8.0, 20° C	78
11.8 µg/L for 48 h	LC50 at pH 8.0, 25° C	78
19.7 µg/L for 24 h	LC50 at pH 8.0, 20° C	78
Mysid shrimp, *Mysidopsis bahia*; 38-77 µg/L	MATC[b]	1
Norway lobster, *Nephrops norvegicus*		
10 µg/L for 30 days; 4.9 cm in length	Copper concentrations were elevated in most tissues, especially ovary (to 393 from 115 mg/kg DW), but not hepatopancreas or external eggs	79
100 µg/L for 14 days	LC100	79
Crab, *Paragrapsus quadridentatus*		
110-250 µg/L for 96 h	LC16-LC84 for larvae	80
170 µg/L for 96 h	LC50 for larvae	80
Freshwater shrimp, *Paratya australiensis*		
15 µg/L, continuous exposure	Mean molt period of 23 days (range 20-27 days) vs. 25 days (18-36 days) for controls	81
40 µg/L for 96 h	LC50	81
Amphipod *Parhallella natalensis*; 72 µg/L for 48 h	LC50	82
Crayfish, *Procambarus clarkii*		
120 µg/L for 20 days	LC50 for larvae	83
1,300 µg/L for 20 days	LC50 for adults; increased copper concentrations at >480 µg/L in gills but not other tissues	83
3,700 µg/L for 20 days	LC50 for embryos	83

Table 5. *Continued.*

Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
Copepod, *Pseudodiaptomus coronatus*; 138 µg/L for 96 h	LC50	1
Barnacle, *Semibalanus balanoides*; 20-90 µg/L for 100 days	Dose-dependent increase in copper loadings in bodies and egg masses	84
Copepod, *Tigriopus japonicus*; 487 µg/L for 96 h	LC50	1
Copepod, *Tisbe furcata*; 37-57 µg/L	MATC[b]	85
Aquatic insects		
Midge, *Chironomus ninevah*; 0, 20, 100, 150 or 200 µg/L for 21 days (eggs through fourth stage larvae)	Statistically significant, dose-dependent decrease in gene activity of salivary gland chromosomes at 20 µg/L and higher	86
Midge, *Chironomus* sp.; 30 µg/L for 96 h	LC50 at 50 mg $CaCO_3$/L	1
Midge, *Tanytarsus dissimilis*; 16.3 µg/L for 10 days	LC50	1
Various species; 25 µg/L for 10 days in outdoor experimental streams	Mayflies were the most sensitive group with 67-100% reduction in numbers; chironomids had 80% reduction, and caddisflies were reduced by 16-30%	87
Annelids		
Ragworm, *Hediste diversicolor*		
5, 10, or 20 µg/L at four salinities and three temperatures; 1-day-old larvae	20 µg/L caused high mortality at all thermosaline regimens tested; some adverse effects noted at lower concentrations	88
247-513 µg/L for 96 h; no sediments in assay containers	LC50's at various thermosaline regimens	89
3,200-4,100 µg/L for 96 h; sediments present in assay containers	LC50's at various thermosaline regimens	89
Oligochaete, *Lumbriculus variegatus*		
130 µg/L for 96 h	LC50 at pH 6.0-6.5	61
500 µg/L for 96 h	LC50 at pH 8.0-8.5	61
Marine worm, *Nereis diversicolor*; 500 µg/L at three salinities and three temperatures	Mortality was greatest at 5‰ salinity (50% dead in 44 h vs. 66-82 h at higher salinities), and at 20° C (50% dead in 32 h vs. 88-106 h at lower temperatures)	90
Echinoderms		
Echinoid, *Echinometra mathaei*; 20 µg/L for 4 days	Skeletal development of larvae suppressed	1
Sea urchin, *Paracentrotus lividus*; 10-20 µg/L for 4 days	Pluteal growth retarded	1
Sea urchin, *Strongylocentrotus nudus*; adults held in seawater containing 25 µg/L for 30 days; resultant embryos reared in uncontaminated seawater for 30 days	Food consumption of adults decreased after day 16; accelerated development of pluteal stages; all developmental stages had increased activities of acid phosphatase	91
Fish		
Topsmelt, *Atherinops affinis*		
53 µg/L for 15 min; sperm	No effect on fertilization in 48 h	92
100 µg/L for 7 days; larvae, age 5-20 days	No effect	93
109 µg/L for 15 min; sperm	Egg fertilization reduced 50% in 48 h	92
123 µg/L for 96 h; larvae	No deaths	92
137 µg/L for 7 days; larvae, age 7-20 days	LC50	93
146 µg/L for 48 h; embryos	50% abnormal development	92
180 µg/L for 7 days; larvae, age 1-3 days	No deaths	93

Table 5. *Continued.*

Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
238 µg/L for 96 h; larvae	LC50	92
365 µg/L for 7 days; larvae, age 0-5 days	LC50	93
Zebrafish, *Brachydanio rerio*		
0.05 µg/L for 16 days; eggs and larvae	Delayed hatch	94
0.25 µg/L for 16 days; eggs and larvae	No deaths	94
1.0 µg/L for 16 days; eggs	<50% hatched	94
1.0 µg/L; adults	No avoidance but inhibition of attraction response to L-alanine	95
50-150 µg/L for 7 days; adults	No adverse effects on survival or behavior; dose-dependent decrease in kidney leucocyte numbers and phagocytic response	96
Goldfish, *Carassius auratus*		
36 µg/L for 96 h	LC50 at 20 mg $CaCO_3$/L	1
300 µg/L for 96 h	LC50 at 52 mg $CaCO_3$/L	1
368 µg/L for 96 h	LC50 at 272 mg $CaCO_3$/L	97
White sucker, *Catostomus commersoni*; 12.9-33.8 µg/L	MATC[b] at 45 mg $CaCO_3$/L	1
Murrel, *Channa punctatus*; 50 or 100 µg/L for 7 days	Liver pathology	98
Catfish, *Clarias* sp.		
27, 55, or 110 µg/L for 8 weeks; whole fish analyzed for total copper at end of exposure	Copper concentrations, in mg/kg DW, were 15.7 for the low-dose group, 21.8 for the 55 µg/L group, and 31.2 for the high-dose group vs. 6.9 DW in controls	99
425 µg/L for 96 h	LC50; nonresistant strain	99
4,301 µg/L for 96 h	LC50; copper-resistant strain	100
African sharp-tooth catfish, *Clarias gariepinus*; Olifants River (water of 32-55 µg/L), South Africa		
767-991 µg/L for 96 h	10-20% dead	101
1,240-1,380 µg/L for 96 h; adults and juveniles	LC50 at 21-28° C	101
Pacific herring, *Clupea harengus pallasi*; 33 µg/L for 6 days; embryos	LC50	1
Common carp, *Cyprinus carpio*; 100 µg/L for 43 days	Skin histopathology	102
Northern pike, *Esox lucius*; 34.9-104.4 µg/L	MATC[b] at 45 mg $CaCO_3$/L	1
Freshwater fishes; eight species; embryos and larvae; 31.7-43.5 µg/L for 30-60 days	Reduced survival	103
Mummichog, *Fundulus heteroclitus*		
1,000 µg/L for 96 h	Renal and lateral line canal lesions	104
1,700-8,000 µg/L for 96 h	LC30-LC50	104, 105
Indian catfish, *Heteropneustes fossilis*		
250 µg/L; 5 h daily for 30 days	Time-dependent increase in adverse effects on blood chemistry, liver metabolism, and respiration	106
5,000 µg/L for 48-96 h	After 48 h, decreased hematocrit, erythrocyte number, and hemoglobin; after 96 h, increased liver glycogen	107, 108
10,500-25,500 µg/L for 72-96 h	LC50	107, 108
Brown bullhead, *Ictalurus nebulosus*		
4, 8, 16, 32, 64, or 104 µg/L for as long as 600 days; blood chemistry analyzed periodically	Some deaths at 104 µg/L; no deaths at lower doses; no adverse biochemical effects at 16 µg/L and lower	109
4 to 512 µg/L for as long as 20 months	Increases in liver and gill copper concentrations in	110

Table 5. *Continued.*

Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
	survivors at 275 µg/L and higher; equilibrium reached within 30 days. Copper levels in blood were the same as in controls	
170 to 190 µg/L for 96 h; juveniles	LC50	110
Channel catfish, *Ictalurus punctatus*; fingerlings		
Exposed for 96 h at 16 mg $CaCO_3$/L		
51-65 µg/L	LC50; chelated copper	111
54-55 µg/L	LC50; nonchelated copper	111
Exposed for 96 h at 239 mg $CaCO_3$/L		
925-1,041 µg/L	LC50; nonchelated copper	111
1,603-1,878 µg/L	LC50; chelated copper	111
Spot, *Leiostomus xanthurus*; 280 (240-330) µg/L for 96 h; adults	LC50	112
Green sunfish, *Lepomis cyanellus*; 937 (686-1,281) µg/L for 96 h	LC50	97
Bluegill, *Lepomis macrochirus*		
21-40 µg/L	MATC[b] at 45 mg $CaCO_3$/L	1, 114
31 µg/L	Consumed 27% fewer prey than controls	113
40-162 µg/L for 90 days; larvae	Reduced survival	114
40-162 µg/L for 24 months; adults	At 162 µg/L, survival was reduced, growth retarded, and spawning inhibited. Maximum copper concentrations, in mg/kg FW, in treated fish (vs. controls) were 13 in gills (3), 480 in liver (7), and 44 in kidneys (22)	114
236-620 µg/L for 96 h; adults	LC50	97, 115
261 µg/L for 7 days, then subjected to a drop in dissolved oxygen over 60 min from 7.8 to 1.3 mg/L and then allowed to recover in copper-free aerated water	No deaths during copper exposure. During hypoxia; 2 of 77 died; survivors had hyperglycemia, lower plasma sodium, lower liver ATP, and higher plasma potassium than did nonexposed controls. Authors concluded that previous copper exposure causes some hypoxia responses to be accentuated in an additive manner	115
1,100 µg/L for 96 h; larvae	LC50	114
4,300 µg/L for 48 h	LC50	116
Atlantic silverside, *Menidia menidia*; 136 µg/L for 96 h; larvae	LC50	1
Tidewater silverside, *Menidia peninsulae*; 140 (110-180) µg/L for 96 h; larvae	LC50	112
Striped bass, *Morone saxatilis*		
50-100 µg/L for 96 h; larvae	LC50 at 68 mg $CaCO_3$/L	1
150 µg/L for 96 h; fingerlings	LC50 at 68 mg $CaCO_3$/L	1
2,680 µg/L for 96 h; fingerlings; 5‰ salinity	LC50	117
7,880-8,080 µg/L for 96 h; fingerlings; 10-15‰ salinity	LC50	117
Cutthroat trout, *Oncorhynchus clarki*		
37 µg/L for 96 h	LC50 at 18 mg $CaCO_3$/L	1
232 µg/L for 96 h	LC50 at 204 mg $CaCO_3$/L	1
Coho salmon, *Oncorhynchus kisutch*		
0, 15, 60, or 90 µg/L for 170 h; yearlings	No deaths; distress noted at 60 and 90 µg/L. Dose-dependent elevation in serum cortisol. When challenged with seawater, copper-exposed salmon had lowered survival and dose-dependent depression in serum chloride levels	118

Table 5. *Continued.*

Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
5-30 µg/L for as long as 172 days; yearlings	Altered downstream migration patterns, lowered gill ATPase activity, and reduced survival. When subjected to >20 µg/L, appetite was depressed for several weeks to months	119
15.1-31.9 µg/L for 96 h; juveniles	LC50	120
18.2 µg/L for 31 days then challenged with seawater	Reduced survival during adaptation to seawater	121
24.6 µg/L for 31 days; fingerlings	Reduced survival; survivors unable to adapt to seawater	121
26 µg/L for 96 h; alevins	LC50 at 25 mg $CaCO_3$/L	1
46 µg/L for 96 h; adults	LC50 at 20 mg $CaCO_3$/L	1
60 µg/L for 96 h; smolts	LC50 at 95 mg $CaCO_3$/L	1
60-74 µg/L for 96 h; yearlings	LC50 at 95 mg $CaCO_3$/L	1, 119
70 or 140 µg/L for 14 weeks; fingerlings	Loss of appetite and reduced growth. Copper concentrations, in mg/kg DW, at end of study for the controls, the 70 µg/L group, and the 140 µg/L group were 2.9, 5.6, and 9.8 in gills, and 5.7, 6.1, and 7.5 in kidneys	122
70 or 140 µg/L for 14 weeks; liver cytosol samples from fingerlings	Copper concentrations in the low molecular weight fractions of the 70 µg/L group were higher than controls after 6 weeks and increased rapidly; those of the 140 µg/L group increased in the first 2-4 weeks then leveled off. Increasing levels of metallothioneins were detected in low molecular weight fractions of copper-exposed salmon. In the high molecular weight fractions, copper concentrations in both groups increased after 8-10 weeks	123
140 or 210 µg/L for 78 h; yearlings	Median survival times were 60 h for the low-dose group and 48 h for the high-dose group; survivors had elevated serum cortisol. Livers were normal but kidney and gill histopathology was evident in both groups	118
220-280 µg/L for 168 h; fingerlings	LC50	122
310 µg/L for 168 h; prior exposure to 70 µg/L for 16 weeks; fingerlings	LC50	122
550 µg/L for 168 h; prior exposure to 140 µg/L for 16 weeks; fingerlings	LC50	122
Rainbow trout, *Oncorhynchus mykiss*		
0.1 µg/L for 1 h	Avoidance by fry	1
7.0 µg/L for 200 h; smolts	LC10	1
8.0 µg/L for 2 h	Depressed olfactory bulbar electrical responses to the standard stimulant L-serine	124
9.0 µg/L for 200 h; swimup stage	LC10	1
11.4-31.7 µg/L	MATC[b] at 45 mg $CaCO_3$/L	1
13.8 µg/L for 96 h; juveniles	LC50	120
19.0 µg/L for 200 h; alevins	LC10	1
20-30 µg/L for 96 h	LC50 at 30-32 mg $CaCO_3$/L	1
21.5 µg/L for 30 days; juveniles	No adverse effects; no altered susceptibility to *Aeromonas hydrophila* infections	125
22 µg/L for 37 to 41 weeks; two groups: age 14 days postfertilization and posthatch. Controls were held in water containing 4 µg/L	Survival of embryo group reduced 30%. Alterations in cell architecture in both treated groups were noted as early as week 8 posthatch. Both groups had irreversible histopathology of the olfactory organ after 7 months; no histopathology in controls. After 8 months, controls preferred their own rearing water but both copper-exposed groups showed no preference; some recovery 2 to 10 weeks after removal from copper	126, 127

Table 5. *Continued.*

Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
36 µg/L for 96 h; alevins	LC50	120
50 µg/L for 24 h; adults	No deaths; some degeneration of sensory receptors	128
50 µg/L for 21 days; juveniles	Rapid and sustained elevation of plasma cortisol levels; altered plasma cholesterol and sodium levels	129
55 µg/L for 28 days; juveniles	Initial inhibition of sodium uptake and whole body sodium content that were normal by day 28. Abnormal liver enzyme activity. Liver copper increased from 23 mg/kg FW at start to 113 mg/kg FW at day 28	164, 165
70 µg/L	Avoidance by juveniles	166
70-514 µg/L for 96 h	LC50 at 194-370 mg $CaCO_3$/L	1
75 µg/L for 24 h	LC50; survivors had complete degeneration of olfactory receptors	128
90 (50-150) µg/L; embryo through posthatch	LC50 at 28 days	162
130-140 µg/L for 24 h	LC50 at pH 6.5-7.5	130
308 µg/L for 24 h in freshwater vs. 400 µg/L for 24 h in 35‰ seawater	All dead in freshwater vs. no deaths in seawater and no major changes in plasma Na^+, Cl^-, K^+, or Ca^{2+}	131
500 or 1,000 µg/L for 2 or 24 h; fingerlings	Gill histopathology in low-dose, low-exposure group; damage more severe with increasing dose and exposure	131
500 µg/L for 9 days; weight 400 g; under conditions of normal and low dissolved oxygen	No signs of respiratory dysfunction; no difference in copper uptake due to dissolved oxygen levels	133
1,200 µg/L for 6 h	LC50	130
4,560 µg/L	Juveniles attracted	166
Fed diet containing 13 or 684 mg/kg ration for 42 days and simultaneously exposed to waterborne-copper concentrations of 5, 32, 55, or 106 µg/L (low-copper diet) or 13, 38, 62, or 127 µg/L (high-copper diet)	No adverse effects on growth, survival, or food conversion efficiency. Elevated dietary copper increased copper concentrations in liver, kidney, gill, and digesta; increasing waterborne-copper concentrations produced increasing copper concentrations in liver and kidney. For fish in the high-copper diet, the diet provided 99% of the liver copper in the 38 µg/L group, 85% in the 62 µg/L group, and 73% in the 127 µg/L group	134
Fed diets containing 25.8 mg/kg DW ration (vs. 15.8 mg/kg DW in controls) for 28 days; equivalent to 69.2 mg/kg fish (130 g) daily	Fish readily ate copper-contaminated food. Elevated copper levels in gill, liver, and muscle. Some food regurgitation on days 20-28	135
Juveniles fed diet containing 200 mg/kg DW for 32 days followed by normal (15.8 mg/kg DW) diet for 12 days	No deaths. After 32 days whole fish contained 1.5 mg/kg FW vs 1.2 at start; copper concentrations were elevated in gill, gut, blood, skin, and mucus, but not in muscle, liver, or kidney. Copper concentrations in gill and kidney tissues were elevated 12 days after exposure, but other tissues were normal	136
Single intravenous injection of 80 µg/kg BW; juveniles, 100-300 g in body weight	Half-time persistence in plasma was 7.2 min for the short-lived component and 3.2 h for the long-lived component. Plasma copper concentration fell from 1.1 mg/L shortly after administration to about 200 µg/L after 7.5 h	137
Chinook salmon, *Oncorhynchus tshawytscha*		
10-38 µg/L for 96 h	LC50 in soft water	1
19 µg/L for 200 h; swimup stage	LC50	1
20 µg/L for 200 h; alevins	LC50	1
26 µg/L for 200 h; smolts	LC50	1
30 µg/L for 200 h; parr	LC50	1

Table 5. *Continued.*

Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
54-60 µg/L for 96 h; fry	LC50	138
78-145 for 24 h; fry	LC50	138
85-130 µg/L for 96 h	LC50 in hardwater	1
Green snakehead, *Ophiocephalus punctatus*; weight 15-18 g		
5,000-7,500 µg/L for 24 h	Sublethal. Disrupted kidney and liver alkaline phosphatase and acid phosphatase activity	139
70,000 µg/L for 48 h	LC50	139
Nile tilapia, *Oreochromis niloticus*		
50, 100, or 200 µg/L for 8 weeks	At end of exposure, whole fish contained 34.7 and 36.1 mg/kg DW in the two lowest-dose groups and 81.0 mg/kg DW in the high-dose group (vs. 17.4 mg/kg DW in controls)	140
964 µg/L for 96 h	LC50	140
Summer flounder, *Paralichthys dentatus*; embryos; 28 µg/L for 96 h	LC50	1
Flounder, *Paralichthys* spp.; juveniles		
6.4 µg/L for 14 days	Interference with calcium metabolism	157
448 µg/L for 14 days	LC50	157
Fathead minnow, *Pimephales promelas*		
2 µg/L for 96 h; larvae	LC50 at pH 5.6 and dissolved organic carbon (DOC) of 0.2 mg/L	141
10.6-18.4 µg/L	MATC[b] at 30 mg $CaCO_3$/L	142
14.5-33.0 µg/L	MATC[b] at 200 mg $CaCO_3$/L	142
15 µg/L for 96 h	LC50 at pH 6.0-6.5	143
23 µg/L for 96 h	LC50 at 20 mg $CaCO_3$/L	1
44 µg/L for 96 h	LC50 at pH 7.0-7.5	143
182 µg/L for 96 h	LC50 at pH 6.9 and dissolved organic carbon of 15.6 mg/L	141
>200 µg/L for 96 h	LC50 at pH 8.0-8.5	143
210 µg/L for 96 h	LC50 at 100 mg $CaCO_3$/L	163
390 µg/L for 96 h	LC50 at 250 mg Ca/CO_3/L	163
430-470 µg/L for 96 h	LC50 in hard water; continuous flow and static assays	142
European flounder, *Platichthys flesus*		
Seawater-adapted; exposure for 42 days; experimentals (170 µg/L) vs. controls (3 µg/L); values in mg/kg DW tissue		
Gill	7.7 vs. 2.7	167
Kidney	13.1 vs. 4.1	167
Liver	640.2 vs. 15.6	167
Muscle	7.7 vs. 2.7	167
Freshwater-adapted; exposure for 37 days; experimentals (15 µg/L) vs. controls (5 µg/L); values in mg/kg DW tissue		
Gill	16.2 vs. 6.5	167
Kidney	28.7 vs. 14.3	167
Liver	295.6 vs. 157.8	167
Muscle	4.9 vs. 1.8	167
Guppy, *Poecilia reticulata*		
36 µg/L for 96 h	LC50 at 20 mg $CaCO_3$/L	1
112-138 µg/L for 96 h	LC50 at 67-82 mg $CaCO_3$/L	1

Table 5. *Continued.*

Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
75-84 µg/L for 96 h	LC50 in soft water; continuous flow and static assays	142
Winter flounder, *Pleuronectes americanus*		
129 µg/L for 96 h; embryos	LC50	1
180 µg/L for 29.1 days; adults	Gill histopathology	144
560-3,200 µg/L for 29.2 days; adults	Copper-induced histopathology of kidney, liver, and gill; reduced food intake	144
Mangrove rivulus, *Rivulus marmoratus*; 1,400 µg/L for 96 h	LC50	145
Air-breathing catfish, *Saccobranchus fossilis*; 56, 100, or 320 µg/L for 28 days	Dose-dependent decrease in red and white blood cell numbers, hemoglobin, and hematocrit; histopathology in gill, skin, spleen, and kidney	146
Atlantic salmon, *Salmo salar*		
2.4 µg/L	Avoidance threshold in laboratory	147
12.8-621.0 µg/L	Dose-dependent inhibition of olfactory response; toxic effect mainly on transduction mechanisms of the olfactory receptor cells	148
16.9-20.6 µg/L	Avoidance threshold in field	147
32-125 µg/L for 96 h	LC50 at 8-20 mg $CaCO_3$/L	1, 147
Brown trout, *Salmo trutta*;		
22.0-43.2 µg/L	MATC[b] at 45 mg $CaCO_3$/L	1
103-148 (91-165) µg/L	LC50 at 48 h, juveniles	159
Brook trout, *Salvelinus fontinalis*		
2.7 (control), 4.5, 6.1, or 9.4 µg/L for two generations	No adverse effects on growth, survival, or reproduction; no elevated copper concentrations in gill, liver, kidney, muscle, or eggs	152
3.4, 5.7, 9.5, 17.4, or 32.5 µg/L for 337 days	No significant changes in blood chemistry except for measurable decrease in plasma glutamic oxalacetic transaminase activity at 17.4 and 32.5 µg/L	149
6-15 µg/L for 2-24 h; yearlings	Increased cough frequency, increased locomotor activity, and decreased feeding response	150
9.5-17.4 µg/L	MATC[b] at 45 mg $CaCO_3$/L and pH 7.5	151
23, 39, or 68 µg/L for 6 or 21 days	At 39 and 68 µg/L, adverse effects on blood chemistry; decreases in plasma chloride and osmolarity	149
100 µg/L for 96 h; age 14 months	LC50	151
Lake trout, *Salvelinus namaycush*; 22.0-42.3 µg/L	MATC[b] at 45 mg $CaCO_3$/L	92
Red drum, *Sciaenops ocellatus*		
250 µg/L for 96 h; juveniles	No deaths	153
520 µg/L for 96 h; juveniles	LC50 at 25° C and 8‰ salinity	153
Pearl dace, *Semotilus margarita*; 1,000-279,000 µg/L for as long as 7 h then transferred to clean water for 48 h	Decreasing survival and coordination with increasing concentration or duration of exposure after exposure to 1,000 µg/L for 6 h, 9,000 µg/L for 1 h, 74,000 µg/L for 0.33 h, or 279,000 µg/L for 0.25 h	154
Walleye, *Stizostedion vitreum*; 13-21 µg/L	MATC[b] at 35 mg $CaCO_3$/L	1
Florida pompano, *Trachinotus carolinus*; 360-510 µg/L for 96 h	LC50	1
Arctic grayling, *Thymallus arcticus*		
2.65 µg/L for 96 h; swimup fry	LC50	120
9.6 µg/L for 96 h; fry	LC50	120
23-131 µg/L for 96 h; alevins	LC50	120
Amphibians		
Marbled salamander, *Ambystoma opacum*; 50 µg/L for 96 h; embryos	97% survival 4 days posthatch	155

Table 5. *Continued.*

Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
American toad, *Bufo americanus*; tadpoles		
10 µg/L	Avoidance	166
930 µg/L	Attraction	166
Fowler's toad, *Bufo fowleri*; 2,696 µg/L for 7 days; embryos	LC50	155
Two-lined salamander, *Eurycea bislineata*; 1,120 µg/L for 48 h; juveniles	LC50	156
Narrow-mouthed toad, *Gastrophryne carolinensis*		
10 µg/L for 4 days; embryos	34% dead 4 days after hatching	155
40 (30-50) µg/L; embryos through posthatch	LC50 (7 days)	162
50 µg/L for 72 h; embryos	LC50	155
Southern gray treefrog, *Hyla chrysoscelis*		
10 µg/L for 96h; embryos	39% dead 4 days after hatching	155
40 µg/L for 7 days; embryos	LC50	155
60 µg/L for 72 h; embryos	LC50	155
Northern leopard frog, *Rana pipiens*		
10 µg/L for 96h; embryos	34% dead 4 days after hatching	155
50 µg/L for 8 days; embryos	LC50	155

[a]1, USEPA 1980; 2, Bartley 1967; 3, Visviki and Rachlin 1994a; 4, Winner and Owen 1991; 5, Schafer et al. 1994; 6, Visviki and Rachlen 1994b; 7, Abalde et al. 1995; 8, Coppellotti 1989; 9, Ahsanullah and Williams 1991; 10, Stokes 1979; 11, Piccinni and Copellotti 1982; 12, Mersch et al. 1993; 13, Harland and Nganro 1990; 14, Janssen et al. 1994; 15, Ferrando et al. 1993; 16, Ferrando and Andreu 1993; 17, Porta and Ronco 1993; 18, Williams and Dusenbery 1990; 19, Huebner and Pynnonen 1992; 20, Jacobson et al. 1993; 21, Cheng 1979; 22, Ebele et al. 1990; 23, Betzer and Yevich 1975; 24, Arthur and Leonard 1970; 25, Belanger et al. 1990; 26, Zaroogian 1979; 27, Okazaki 1976; 28, Coglianse and Martin 1981; 29, Mathew and Menon 1993; 30, Kraak et al. 1992; 31, Kraak et al. 1994; 32, Hameed and Raj 1989; 33, Raj and Hameed 1991; 34, Bordin et al. 1994; 35, Roper and Hickey 1994; 36, Zaroogian et al. 1992; 37, Chelomin and Belcheva 1992; 38, Eisler 1977; 39, Sanders et al. 1991; 40, Calabrese et al. 1984; 41, Sanders et al. 1994; 42, Stromgren and Nielsen 1991; 43, Hole et al. 1993; 44, Gainey and Kenyon 1990; 45, MacKenzie 1961; 46, Viarengo et al. 1981; 47, Viarengo et al. 1990; 48, Davies 1992; 49, Krishnakumar et al. 1990; 50, Winger et al. 1984; 51, Paulij et al. 1990; 52, Mule and Lomte 1994; 53, Soria-Dengg and Ochavillo 1990; 54, Suresh and Mohandas 1993; 55, Jacobson et al. 1993; 56, Koivisto et al. 1992; 57, Neff and Anderson 1977; 58, Zia and Alikhan 1989; 59, Nonnotte et al. 1993; 60, Scott-Fordsmand and Depledge 1993; 61, Schubauer-Berigan et al. 1993; 62, Ericksson and Weeks 1994; 63, Mukhopadhyay et al. 1994; 64, Enserink et al. 1991; 65, Lazorchak and Waller 1993; 66, Roux et al. 1993; 67, Ingersoll and Winner 1982; 68, Dobbs et al. 1994; 69, Maund et al. 1992; 70, Martin et al. 1989; 71, Borgmann et al. 1993; 72, Collyard et al. 1994; 73, West et al. 1993; 74, Natarajan et al. 1992; 75, Vijayaraman and Geraldine 1992; 76, Clements et al. 1990; 77, Wong et al. 1993; 78, Zou and Bu 1994; 79, Canli and Furness 1993; 80, Ahsanullah and Arnott 1978; 81, Daly et al. 1992; 82, Bhat and Vamsee 1993; 83, Rice and Harrison 1983; 84, Powell and White 1990; 85, Bechmann 1994; 86, Aziz et al. 1991; 87, Clements et al. 1992; 88, Ozoh and Jones 1990; 89, Ozoh 1992a; 90, Fernandez and Jones 1990; 91, Durkina and Evtushenko 1991; 92, Anderson et al. 1991; 93, McNulty et al. 1994; 94, Dave and Xiu 1991; 95, Steele et al. 1990; 96, Rougier et al. 1994; 97, Johnson and Finley 1980; 98, Khangarot 1992; 99, Daramola and Oladimeji 1989; 100, Ebele et al. 1990; 101, van der Merwe et al. 1993; 102, Iger et al. 1994; 103, McKim et al. 1978; 104, Eisler and Gardner 1973; 105, Lin and Dunson 1993; 106, Singh and Reddy 1990; 107, Banerjee and Homechaudhuri 1990; 108, Srivastava 1982; 109, Christensen et al. 1972; 110, Brungs et al. 1973; 111, Straus and Tucker 1993; 112, Mayer 1987; 113, Sandheinrich and Atchison 1989; 114, Benoit 1975; 115, Heath 1991; 116, Dobbs et al. 1994; 117, Reardon and Harrell 1990; 118, Schreck and Lorz 1978; 119, Lorz and McPherson 1977; 120, Buhl and Hamilton 1990; 121, Stevens 1977; 122, Buckley et al. 1982; 123, McCarter et al. 1982; 124, Hara et al. 1977; 125, Snarski 1992; 126, Saucier et al. 1991a; 127, Saucier et al. 1991b; 128, Klima and Applehans 1990; 129, Munoz et al. 1991; 130, Shaw and Brown 1974; 131, Wilson and Taylor 1993; 132, Kirk and Lewis 1993; 133, Pilgaard et al. 1994; 134, Miller et al. 1993; 135, Handy 1993; 136, Handy 1992; 137, Carbonell and Tarazona 1994; 138, Hamilton and Buhl 1990; 139, Srivastava and Pandey 1982; 140, Daramola and Oladimeji 1989; 141, Welsh et al. 1993; 142, Mount and Stephan 1969; 143, Schubauer-Berigan et al. 1993; 144, Baker 1969; 145, Lin and Dunson 1993; 146, Khangarot and Tripathi 1991; 147, Sprague et al. 1965; 148, Winberg et al. 1992; 149, McKim et al. 1970; 150, Drummond et al. 1973; 151, McKim and Benoit 1971; 152, McKim and Benoit 1974; 153, Peppard et al. 1991; 154, Tsai 1979; 155, Birge and Black 1979; 156, Dobbs et al. 1994; 157, Dodoo et al. 1992; 158, Koivisto and Ketola 1995; 159, Marr et al. 1995; 160, Eisler 1995; 161, Suresh et al. 1993; 162, Birge 1978; 163, Benson and Birge 1985; 164, Lauren and McDonald 1987a; 165, Lauren and McDonald 1987b; 166, Birge et al. 1993; 167, Stagg and Shuttleworth 1982.

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

Table 6. Effects of copper on selected birds.

Organism, copper dose, and other variables	Effects	Reference[a]
Mallard, *Anas platyrhynchos*		
Fed diets containing 15 or 135 mg/kg ration for 18 days; ducklings	Livers from low-dose group had 30 mg/kg dry weight (DW) at day 4 and 107 mg/kg at day 18; values for the high-dose group were 45 mg/kg at day 4, 74 mg/kg at day 7, and 254 mg/kg DW at day 18	1
For 15 days adults were given a choice of distilled water or water with 30, 60, or 100 mg/L	Ducks consumed significantly more water treated at 100 mg/L than distilled water; no preference was evident at lower doses	2
Ducks, *Anas* spp.		
Ducklings fed diets containing 15 or 50 mg/kg ration for 51 days	Livers from control ducklings had 9.3 mg/kg DW. Livers from both treated groups had about 17 mg/kg DW at day 9, 37 mg/kg at day 30, and 47 mg/kg DW at day 51	1
Ducklings fed diet containing 200 mg/kg DW ration for 58 days	Copper concentrations in livers increased from 23 mg/kg DW at day 23 to 141 mg/kg DW at day 44; at day 58 it had declined to 80 mg/kg DW	1
Domestic chicken, *Gallus* spp.		
Chicks age 1-day fed copper-deficient diet of 0.7 mg/kg ration or copper-adequate diet of 8.0 mg/kg ration for 4-6 weeks	Chicks fed copper-deficient diet had >50% mortality and high frequency of cardiovascular and skeletal lesions. Chicks on copper-adequate diet had negligible mortality, no histopathology, and normal growth	3, 4
Chicks fed diet containing 1.5 mg/kg ration for 60 days	95% dead of copper deficiency	5
Chicks fed diet containing 2.7 mg/kg ration for 60 days	Normal growth but high frequency of vascular rupture	5
Chicks fed diet containing 8.7 mg/kg feed for 60 days	Good survival and growth	5
Day-old chicks fed diets containing 10 (control), 100, 200, or 350 mg/kg ration for 25 days	Reduced weight gain in the 350 mg/kg group; other groups same as controls	6
Chicks fed diets containing 15 or 50 mg/kg ration for 51 days	Livers from controls had 5.9 mg/kg DW; treated groups were similar to controls, with copper concentrations in livers between 4.3 and 8.5 mg/kg DW	1
Adults were fed diets equivalent to 28 mg/kg body weight (BW) daily for the first week, 42 mg/kg BW daily for week 2, and 100 mg/kg BW daily until anemia, toxicosis, or death occurred	After 2 to 6 weeks, chickens were weak, anorectic, and lethargic; 35% were anemic	6
Chicks fed diet containing 200 mg/kg DW for 58 days	Maximum copper concentration in liver was 17.2 mg/kg DW at day 20; by day 58 it had dropped to 7.2 mg/kg DW	1
Chicks fed diets supplemented with 250, 500, or 1,000 mg/kg ration for 4 weeks	No gizzard erosion in controls; chicks fed the 250 mg/kg diet grew better than other treated groups but some had gizzard erosion. Chicks fed the 500 and 1,000 mg/kg diets had decreased growth, decreased feed efficiency, and a high frequency of gizzard erosion. Severity of gizzard erosion was significantly reduced in the 500 mg/kg group (but not the 1,000 mg/kg group) by adding 0.35% cholic acid	7
Laying hens fed diets supplemented with 250, 500, 1,000, or 2,000 mg/kg ration for 48 days	Controls and the 250 mg/kg group had lower concentrations of copper in liver than those fed diets containing 500 mg/kg and higher. Copper concentration in the 2,000 mg/kg group increased from 3 mg/kg DW at day 3 to 1,790 mg/kg DW at day 48 (vs. 11.3 mg/kg DW in controls)	8
Turkey, *Meleagris gallopavo*		
Day-old poults fed diets containing 0, 60, 120, or 240 mg/kg ration and adequate	Diets containing 60 mg/kg improved body weight at age 8 weeks; the 120 and 240 mg/kg diets inhibited	9

Table 6. *Continued.*

Organism, copper dose, and other variables	Effects	Reference[a]
levels of methionine for 24 weeks	growth for the first 8 weeks but not during the next 16 weeks	
Week-old poults fed a purified corn starch, isolated soy protein diet supplemented with 50 to 800 mg/kg ration for 3 weeks	Dose-dependent increase in mortality and decrease in growth	10
Week-old poults fed corn-soybean meal supplemented with 100 to 800 mg/kg ration	No adverse effects on survival; growth reduced only at 800 mg/kg diet	10
Day-old poults fed diet containing 500 mg/kg ration for 24 weeks	Reduced growth and increased gizzard histopathology	9

[a]1, Wood and Worden 1973; 2, Rowe and Prince 1983; 3, Carlton and Henderson 1963; 4, Carlton and Henderson 1964a; 5, Carlton and Henderson 1964b; 6, National Academy of Sciences 1977; 7, Poupoulis and Jensen 1976; 8, Stevenson and Jackson 1978; 9, Kashani et al. 1986; 10, Supplee 1964.

Copper is lethal to mammals through a variety of routes (Table 7). Single oral doses of 6-637 mg Cu/kg BW are fatal to humans. A single oral dose of 200 mg/kg BW is usually fatal to cattle. Dietary copper is lethal when eaten for extended periods at more than 80 mg Cu/kg ration in sheep (equivalent to 5.1-10.7 mg Cu/kg BW daily), more than 238 mg/kg ration in pigs, and more than 4,000 mg/kg ration in rats (equivalent to more than 133 mg Cu/kg BW daily; Table 7). Adverse sublethal effects of copper to sensitive mammals occur in human infants at drinking water concentrations more than 3 mg Cu/L; in cattle at dietary levels greater than 20 mg Cu/kg BW by way of intraperitoneal injection and more than 4.2 mg Cu/kg BW via drinking water; in sheep given daily oral doses of 7.5 to 15.0 mg Cu/kg BW or fed diets containing more than 37.3 mg Cu/kg ration; in rats at greater than 100 mg Cu/kg ration (equivalent to greater than 7.9 mg Cu/kg BW daily), greater than 400 mg Cu/L drinking water, or greater than 2.0 to 2.5 mg Cu/kg BW daily via injection; and in pigs at more than 14.5 mg Cu/kg BW daily via diet. Elevated copper concentrations (328 mg Cu/kg DW) occur in livers of surviving cattle fed diets containing 8.2 mg Cu/kg ration; of sheep (1,109 mg/kg DW liver) fed diets containing 37.3 mg Cu/kg ration; and of rats (710 mg/kg FW liver) given intraperitoneal injections of 3.75 mg Cu/kg BW daily for 18 weeks (Table 7).

Table 7. Effects of copper on selected mammals.

Organism, copper dose, and other variables	Effects	Reference[a]
Cattle, *Bos* spp.		
Fed diet containing 8.2 mg/kg ration for 333 days	Copper concentration in liver increased from 111 to 328 mg/kg dry weight (DW)	1
Fed diets containing 20 to 125 mg/kg ration for extended period	Intoxication	2
Single dose; 200 mg/kg body weight (BW)	Lethal	2
Horses, *Equus* sp.		
Horses given a single oral dose of 20 or 40 mg/kg BW were challenged 24 h later with oral doses of 2, 4, 6, or 8 mg selenium/kg BW	All horses given 20 or 40 mg/kg BW were unaffected by selenium, regardless of dosage; without copper pretreatment, signs of severe Se toxicosis—including lethargy, colic, and death—developed in horses given 6 or 8 mg Se/kg BW	3
Fed diet containing 800 mg/kg ration for 6 months	No adverse effects	4
Humans, *Homo sapiens*		
3 mg/L drinking water for 9 months	Liver damage in infants	5
30 mg/L drinking water; single exposure; total intake unknown	Vomiting, diarrhea, stomach cramps	5

Table 7. *Continued.*

Organism, copper dose, and other variables	Effects	Reference[a]
6 to 637 mg/kg BW; single exposure (attempted suicides)	13 of 53 patients died; death attributed to shock and hepatic or renal complications	5
Children who died from Wilson's disease vs. normal children		
Brain	2,090 mg/kg ash weight (AW), equivalent to 31 mg/kg fresh weight (FW) or 129 mg/kg DW vs. 290 mg/kg AW	6
Heart	6,800 mg/kg AW, equivalent to 75 mg/kg FW or 298 mg/kg DW vs. 340 mg/kg AW	6
Kidney	27,160 mg/kg AW, equivalent to 299 mg/kg FW or 1,245 mg/kg DW vs. 250 mg/kg AW	6
Liver	74,570 mg/kg AW, equivalent to 820 mg/kg FW or 2,217 mg/kg DW vs. 1,300 mg/kg AW	6
Pancreas	1,200 mg/kg AW vs. 160 mg/kg AW	6
Spleen	1,930 mg/kg AW vs. 100 mg/kg AW	6
Mice, *Mus* spp.		
Strain genetically deficient in copper (Menkes disease) given subcutaneous injections of 50 µg copper chloride ($CuCl_2$) on postnatal days 7 and 10. Before therapy, liver copper concentration was 3.1 mg/kg FW (vs. 30.1 mg/kg FW in normal mice)	Seven months postinjection there was some reduction in neurodegeneration; copper was distributed normally in liver; in intestine, copper accumulated in histiocytes	7
120 µg/m³ air for 1-2 weeks	Alveoli thickening	5
<3.3 mg/kg BW; single intraperitoneal (ip) injection	No effect on oxygen consumption or body temperature	8
3.3-8.0 mg/kg BW; single ip injection	Dose-dependent reduction in oxygen consumption and body temperature	8
4.02 mg/kg BW; single ip injection	50% dead	8
Drinking water equivalent of 4.2 mg/kg BW daily for 850 days	Decreased growth and survival	5
Drinking water equivalent of 42.5 mg/kg BW daily as copper glutamate; lifetime exposure	Maximal lifespan reduced from 986 days to 874 days	5
640 mg/L drinking water for 850 days	Decreased survival	5
Mink, *Mustela vison*		
Dietary equivalent of 3.5 mg/kg BW daily for 50 weeks	Decreased survival (deficiency)	5
Dietary equivalent of 13.5 mg/kg BW daily for 50 weeks	Some deaths; no adverse effect on reproduction of survivors	5
Rabbit, *Oryctolagus* sp.		
600 µg/m³ air for 4 to 6 weeks	No adverse systemic or immunological effects	5
Domestic sheep, *Ovis aries*		
Ewes were fed a copper-deficient diet of 1.3 to 2.5 mg/kg DW ration. At mating, livers contained 20 to 106 mg/kg DW; after lambing, livers contained 3 to 12.3 mg/kg DW	22 of 54 (41%) lambs from ewes fed a copper-deficient diet developed swayback; these lambs had liver concentrations of 5.9 (1.5-11.0) mg/kg DW vs. 6.9 (2.5-14) mg/kg DW in non-swaybacked lambs	11
Ewes from vicinity of copper production plant receiving daily dietary intake of 465 mg/ewe (10.7 mg/kg BW daily) vs. control ewes with average daily dietary intake of 29 mg/ewe (0.67 mg/kg BW daily)	All ewes near copper facility were dead by day 89 vs. none dead in controls. At day 35, ewes near copper production plant had 11.8 mg/kg DW in wool vs. <7 mg/kg DW in controls	9
Merino sheep, 6 to 9 months old; given 5.1 mg/kg BW 5 times weekly for 28 weeks through the mouth as copper sulfate. Heliotrope and nonheliotrope diets	Some deaths. Yellow discoloration of sclera of eye; passing of red-colored urine. Copper concentrations, in mg/kg DW, from sheep fed nonheliotrope diets were 1,394 in liver (824 in controls) and 132 in kidney (20 in controls). Sheep on heliotrope diet had 2,783 mg/kg DW in liver and 321 mg Cu/kg DW in kidney	10

Table 7. *Continued.*

Organism, copper dose, and other variables	Effects	Reference[a]
Oral administration of 7.5 mg/kg BW daily for 83 days, as copper sulfate	Severe morphological changes in liver, kidney, and brain; tissue damage continued after cessation of copper and was sufficiently severe to lead to repeated hemolytic crises. Maximum copper concentrations at day 83 were 3,289 mg/kg DW in liver (138 in controls), and 683 in kidney (15 in controls)	12
Lambs fed diets containing 9.1 (control) or 37.3 mg/kg ration for 11 weeks	Normal growth and survival. At slaughter, liver copper concentrations, in mg/kg DW, were 372 in controls and 1,109 in the treated group; plasma aspartate aminotransferase was elevated in the high-dose group	13
Lambs fed diets containing 11 (control), 18, or 25 mg/kg ration for 10 weeks	Survival and growth normal in all groups. Liver concentrations, in mg/kg DW, were 239 (11 mg/kg group), 454 (18 mg/kg group), and 721 (25 mg/kg group)	13
Rams, age 4.5 to 5.5 years; daily intake of 15 mg/kg BW for 50 days	Increased concentrations of copper in ejaculates (16 mg/kg DW vs. 2 in controls) and liver (1,435 mg/kg DW vs. 63). Sperm motility in test rams was significantly decreased, abnormalities were increased, and testes copper was elevated (96-101 mg/kg DW vs. 60-69 in controls)	14
Equivalent of 20 mg/kg BW daily for 9 weeks	Hemolysis	15
Lambs fed diet containing 80 mg/kg DW ration for 6 weeks	Postmortem examination of 17 lambs that died suddenly showed brain histopathology, particularly in white matter of midbrain, pons, and cerebellum. Severe liver cirrhosis and necrosis of kidney tubules. Liver copper elevated at 3,225 to 4,325 mg/kg DW	16
Laboratory white rat, *Rattus* sp.		
Dietary route		
Male weanlings fed copper-deficient (0.13 mg/kg ration) or copper-adequate (5.7 mg/kg ration) diets for 49 days	24% of the copper-deficient rats died of cardiac rupture; ruptured hearts had lower magnesium and higher sodium, phosphorus, and calcium. Copper-adequate rats had 21.7 mg/kg DW liver vs. 2.2 in copper-deficient rats in which hearts had ruptured	17
Low copper diet of 1 mg/kg DW ration vs. 5 mg/kg diet for 12 weeks	Dose-dependent increase in copper concentrations in kidney, liver, and plasma. Low Cu status increases retention of cadmium in liver	18
100 mg/kg diet for 20 weeks	Increased blood pressure	5
250 mg/kg diet for 3 months	No deaths	5
500 mg/kg diet for 3 months	Kidney damage	5
1,000 mg/kg diet for 3 months	Stomach and liver damage	5
2,000 mg/kg diet for 1 to 3 weeks	Liver and kidney damage	5
4,000 mg/kg diet (133 mg/kg BW daily) for 1 week	Increased mortality	5
6,000 mg/kg diet (300 mg/kg BW daily) for 2 weeks	Weanlings died from extensive centrilobular necrosis	5
Equivalent to 7.9 mg/kg BW daily for 90 days	Increased serum glutamic oxaloacetic transaminase enzyme activity	5
Equivalent to 10 mg/kg BW daily for 20 weeks	Increased blood pressure; increased hemoglobin	5
Equivalent to 40 mg/kg BW daily for 30 days	Anemia, increased liver enzyme activity, increased cholesterol and urea	5
Equivalent to 130 mg/kg BW daily for 18 weeks	Decreased body growth; decreased testes weight	5
Equivalent to 144 mg/kg BW daily for 4 weeks	Decrease in rate of body weight gain	5
Drinking water route		
0.25, 2, or 16 mg/L for 109 to 119 days	Serum copper rose from 44 µg/L (controls) to 106 µg/L (0.25 mg/L group) to 848 (2 mg/L) to 943 µg/L (16 mg/L	19

Table 7. *Continued.*

Organism, copper dose, and other variables	Effects	Reference[a]
	group); dose-dependent decrease in serum cholesterol, triglycerides, and phospholipids	
50 or 150 mg/L for 15 to 30 days	No adverse effect on liver microsomal activity	20
398 to 450 mg/L for 15 to 30 days	Reduction in liver aniline hydroxylase activity; liver histopathology	5, 20
Inhalation route		
Copper sulfate spray containing 330 g/L for daily exposures of 1 h for as long as 10 days	Concentrations of copper in liver, in mg/kg FW, were 32 after 6 hr, 84 after 5 days, and 285 after 10 days	27
Injection route		
0.26 mg/rat daily as copper sulfate for 60 days; subcutaneous (sc) injection	Treated rats had 1,000 mg/kg FW liver (vs. 4.7 in controls); lowered hemoglobin, hematocrit, and red cell counts; mean survival time of 67 days; hepatic and renal histopathology	15
0.625, 1.25, 2.5, or 3.75 mg/kg BW daily for 18 weeks; intraperitoneal injection	Dose-time-dependent increase in copper concentrations in liver, spleen, and lung; little accumulation in muscle and skin. Reduced growth at 2.5 and 3.75 mg/kg BW daily; reduced survival at 3.75 mg/kg BW. Maximum copper concentrations recorded, in mg/kg FW (vs. saline controls,) were 710 in liver (<5), 212 in kidney (<10), 7 in lung (<1.5), 27 in spleen (<2.0), 6 in bone (<2.0), and 2.2 in testes (<1.6)	21
Adult males given 2 mg/kg BW daily as copper acetate for 14 days; intraperitoneal injection	Increased serum ceruloplasmin and white blood cell number	22
Other routes		
Isolated cells from adrenal and testes held in media containing 0.065, 0.65, or 6.5 mg/kg for 2 h	No effect at lowest doses. High dose caused decreased survival of cells from both organs and reduced testosterone production	23
Rodents, various species		
3-7 mg/kg BW; single ip or sc injection	50% dead	15
Common shrew, *Sorex araneus*		
Newly weaned shrews fed diets equivalent to 2.13 mg/shrew daily for 12 weeks; uncontaminated diets contained 25.1 mg/kg DW ration	No effect on growth, survival, or tissue copper burdens; kidney and liver copper concentrations increased in response to cadmium dosing	24, 25
Domestic pig, *Sus* spp.		
Dietary equivalent of 14.6 mg/kg BW daily for 54 days	Decreased hemoglobin and hematocrit; decreased growth rate	5
Dietary equivalent of 36 mg/kg BW daily for 7 weeks	Decreased hemoglobin, altered serum enzyme activity	5
Fed diets containing <150 mg/kg ration for 9 months	No copper accumulations over controls in liver (16-48 mg/kg DW) or kidney (20-49 mg/kg DW); growth promoting effects	26
Fed diets supplemented with 238-250 mg/kg ration, as copper sulfate, from age 3 weeks for 9 months	High mortality, usually between age 14 and 20 weeks. Dead pigs had 1,300 mg/kg DW in liver and 95 mg/kg in liver; survivors had as much as 2,100 mg/kg DW liver, 670 mg/kg DW kidney, and 3.3 mg/L serum	26
Fed diets containing 700 mg/kg ration for several months	High mortality; survivors had anemia, gastric ulcers, liver pathology, and 100-170 mg/kg FW in liver	15

[a]1, Miltmore et al. 1978; 2, Gummow et al. 1991; 3, Stowe 1980; 4, Bremner 1979; 5, ATSDR 1990; 6, Schroeder et al. 1966; 7, Yoshimura et al. 1995; 8, Gordon et al. 1990; 9, Bires and Vrzgula 1990; 10, Howell et al. 1991; 11, Lewis et al. 1967; 12, Gopinath and Howell 1975; 13, Buckley and Tait 1981; 14, Gamcik et al. 1990; 15, Aaseth and Norseth 1986; 16, Doherty et al. 1969; 17, Saari et al. 1994; 18, Panemangelore 1993; 19, Petering et al. 1977; 20, Moffitt and Murphy 1973; 21, Lal and Sourkes 1971; 22, Jehan and Motlag 1994; 23, Ng and Liu 1990; 24, Dodds-Smith et al. 1992a; 25, Dodds-Smith et al. 1992b; 26, Higgins 1981; 27, Romeu-Moreno et al. 1994.

Terrestrial Plants and Invertebrates

Copper is toxic to sensitive plants when plant nutrient solutions contain greater than 40-200 µg Cu/L, when leaves have greater than 10 to 12 mg Cu/kg DW, and when extractable copper in soils is greater than 60 mg/kg DW soil (Table 4). Excess copper inhibits root elongation and branching and reduces the ability of the plant to explore the soil for water and nutrients (Arduini et al. 1995). Root damage occurs in pine seedlings (*Pinus* spp.) after exposure for 10 days to nutrient solutions that contain 40 µg Cu/L. A lower concentration of 4 µg Cu/L has no adverse effects on root growth and morphology, while a higher concentration of 400 µg Cu/L completely inhibits root growth within 3 days (Arduini et al. 1995). Poultry litter is a useful agricultural byproduct with high nitrogen and phosphorus content and is frequently added to agricultural soils. Poultry litter from northern Georgia containing 1,196 mg Cu/kg DW and applied at a final rate of 5-15 mg Cu/kg soil to fields of Sudex (*Sorghum bicolor* x *S. sudanense*) did not affect copper levels of treated Sudex or produce any evidence of toxicity (van der Watt et al. 1994). But most terrestrial vegetation in the United States, Sweden, Wales, and other locales is usually adversely affected by emissions from copper mines, brass foundries, and copper smelters (Hutchinson 1979). Damage to vegetation persists for at least 50 years after closure of a copper smelter because of copper, arsenic, and lead in the soil. Particularly sensitive to copper in the soils are white pine (*Pinus strobus*) and red maple (*Acer rubrum*); less sensitive are Douglas fir (*Pseudotsuga menziesii*) and lodgepole pine (*Pinus contorta*; Hutchinson 1979).

Earthworms (*Eisenia fetida*) held in soils containing 53 mg Cu/kg DW show a 50% reduction in cocoon production in 56 days; 32 mg Cu/kg soil had no effect on cocoon production (Spurgeon et al. 1994). The LC50 (56 days) value for earthworms is 555 mg Cu/kg DW soil; no deaths occur at 210 mg/kg soil during this period. Copper is more toxic to *Eisenia fetida* than are salts of cadmium, zinc, or lead (Spurgeon et al. 1994). Copper adversely affects the earthworm *Lumbricus rubellus* (Ma 1984). Concentrations of 150 mg Cu/kg surface soil from an accidental spill of copper sulfate in grasslands reduced earthworm populations by about 50%; surface soil concentrations of 260 mg Cu/kg kill almost 100% of the *Lumbricus*. Copper is most toxic to *Lumbricus* at low soil pH (4.8-7.1) and at low temperatures (Ma 1984).

Tests show that the presence of soil reduces the toxicity of copper to the soil-dwelling nematode *Caenorhabditis elegans*; copper toxicity to nematodes increases with increasing densities of bacteria and increasing concentrations of sodium chloride or potassium chloride (Donkin and Dusenbery 1993). Terrestrial isopods efficiently assimilate and store copper as detoxified granules in the hepatopancreas; this activity is in contrast to many species of marine crustaceans that are unable to assimilate, detoxify, or otherwise regulate copper (Weeks and Rainbow 1993).

Aquatic Organisms

Plants

Photosynthesis and growth in sensitive species of freshwater algae are inhibited by copper concentrations of 1-6 µg/L (NAS 1977; Table 5). For sensitive species of estuarine phytoplankton, copper is lethal at 50 µg/L and most toxic under conditions of decreasing salinity, pH, and concentrations of chelators (Erickson et al. 1970). Sensitivity to copper varies widely among species of estuarine algae (Erickson et al. 1970; Table 5); some species, for example, grow normally at concentrations as high as 10 mg Cu/L during exposure for 9 days (Piccinni and Copellotti 1982). In mesocosm studies, 50 µg Cu/L caused a reduction of about 80% in total zooplankton and total algal biovolumes; the algal assemblage that persisted was dominated by diatoms (Havens 1994). Copper-resistant strains of *Euglena gracilis* challenged with high sublethal concentrations of copper for 5 days had an altered cysteine metabolism (Coppellotti 1989).

Some species of aquatic plants absorb or adsorb dissolved copper at extremely high rates (Table 5). Bioconcentration factors for copper and freshwater alga (*Chlorella* sp.) range from 203-2,000 after exposure for 14 to 30 h (USEPA 1980). Seagrass (*Heterozostera tasmanica*) in seawater containing 42 µg Cu/L for several weeks contain 2,700 mg Cu/kg DW; seagrasses in media containing 0.3 µg Cu/L contain 2.5 mg Cu/kg DW; and intermediate values are reported for 10 µg Cu/L (306 to 564 mg/kg DW) and 20 µg/L (1,280 mg/kg DW; Ahsanullah and Williams 1991). Some freshwater aquatic macrophytes accumulate as much as 54,500 mg Cu/kg DW, as was the case for *Lemna* sp. during exposure to 1,000 µg Cu/L; a lower dose regimen of 35 µg Cu/L results in 256 mg Cu/kg DW *Lemna* (Stokes 1979).

Cnidarians

Sea anemones (*Anemonia viridis*) in seawater solutions containing 50 or 200 µg Cu/L regulate copper by expelling zooxanthellae which are shown to accumulate copper (Harland and Nganro 1990).

Mollusks

Initial effects of copper on mussels (*Mytilus* spp.) include valve closure, a reduction in filtration rates, and cardiac inhibition; these responses all serve to slow the uptake of copper through a reduction in mussel contact with the ambient environment and a reduction in blood flow within the organism (Gainey and Kenyon 1990). Copper impairs the structure and function of cellular membranes in mussels by stimulating the peroxidation of membrane lipids; end products of lipid peroxidation contribute to the formation of lipofuscins (Viarengo et al. 1990).

Copper-induced lysosomal lipofuscin accumulations, together with metallothioneins, control copper residues at the cellular levels and are responsible for the short half-time persistence (6 to 8 days) of copper in the digestive gland of mussels (Viarengo et al. 1990). Concentrations of heat shock protein (hsp60) in mantle tissues of mussels exposed to copper increased in a dose-dependent manner; hsp60 may have potential as a biomarker of copper insult (Sanders et al. 1991). Copper-stressed common mussels (*Mytilus edulis*) die more quickly under conditions of anoxia, high temperatures, and low salinities (Weber et al. 1992). Concentrations of copper that cause a decrease in yields of normal larvae in populations of *Mytilus edulis* from unpolluted or mildly contaminated sites did not affect embryonic development of mussels from polluted sites; cross breeding of mussels from these sites suggests that copper tolerance in mussels is mostly maternally determined (Hoare et al. 1995a). Embryos of common mussels are more sensitive to copper than veliger larvae or postlarval spat stages (Hoare et al. 1995b). A copper-induced decrease in glochidial viability is a possible explanation for the disappearance of freshwater unionid mussels from acid- and metals-contaminated waters (Huebner and Pynnonen 1992). Hole et al. (1993) state that mussels of all ages are equally susceptible to copper and that their capacity to recover declines with increasing age; however, this phenomenon needs verification.

Bioconcentration factors for marine bivalves (ratio of milligrams of copper per kilogram fresh weight soft parts to milligrams of copper per liter of medium) vary from 85 to 28,200. Bioconcentration factors for copper are highest for American oysters after exposure for 140 days (20,700-28,200), and lowest for bay scallops (*Argopecten irradians*) after exposure for 112 days (3,310) and for softshell clams after exposure for 35 days (3,300; USEPA 1980). Copper is more toxic to embryos of the tropical giant clam (*Tridacna derasa*) than to embryos of bivalves from temperate regions (Soria-Dengg and Ochavillo 1990), possibly because many tropical species of shellfish live near their upper lethal thermal limits and are unable to withstand additional environmental stressors. Juveniles of Asiatic clams (*Corbicula fluminea*) are more sensitive than adults to ionic copper (Belanger et al. 1990).

On exposure to lethal concentrations of copper the channeled whelk (*Busycon canaliculatum*), a marine gastropod, accumulates the metal in gill and osphradium. These tissues show progressive histopathology including swelling of the gill filaments, amoebocytic infiltration of the connective tissue, and necrosis and sloughing of the mucosa (Betzer and Yevich 1975). Copper-resistant strains of freshwater gastropods are found in media containing elevated concentrations of 35 µg Cu/L (Ebele et al. 1990), suggesting physiological or genetic adaptation. Fine suspensions of copper and kaolinite mixtures are more toxic to freshwater gastropods than copper alone; toxicity is greater at pH 8 than at pH 7 (Al-Sabri et al. 1993). The authors conclude that copper is strongly adsorbed by kaolinite in alkaline media and that the acidic pH of the snail gut enhances release of ionic copper. In freshwater gastropods, ionic copper causes hypersynthesis of lysosomal enzymes and acid and alkaline phosphatases; immature gastropods are more sensitive than adults (Winger et al. 1984).

Arthropods

Life-cycle exposures of four daphnid species to graded concentrations of copper show reductions in survival at more than 40 µg/L and reductions in growth and reproduction at 40 to 60 µg/L; heavier and larger species are the most resistant to copper (Winner and Farrell 1976; Table 5). Starvation increases the sensitivity of most species of freshwater cladocerans to copper (Koivisto et al. 1992); however, there is no difference in LC50 (48 h) values between fed and starved *Daphnia magna* (Lazorchak and Waller 1993). Bioavailability and toxicity of copper to *D. magna* and other tested arthropods are usually higher under conditions of increasing acidification, ionic copper, alkalinity, and temperature, or of decreasing dissolved organic carbon (Meador 1991; Taylor et al. 1994; Zou and Bu 1994). Mixtures of copper and other metals produce additive or more-than-additive effects in *D. magna* than would be expected on the basis of individual components (Enserink et al. 1991). The concept that chronic exposures to pulses of the LC50 concentrations of copper or cadmium causes no damage to freshwater organisms—provided that the average daily concentration never exceeds the no-observable-effect concentration—was tested in daphnids. The concept was true for cadmium but not copper, and the use of pulsed exposures for establishing water quality criteria to protect aquatic life needs to be reexamined (Ingersoll and Winner 1982).

Copper uptake by aquatic arthropods occurs usually by way of the gut after eating or from the gills and other permeable surfaces in contact with the ambient medium (Weeks and Rainbow 1993). Copper accumulations by crustaceans are greatest at elevated (summer) temperatures and during molting (Powell and White 1990). A relatively high bioconcentration factor of 2,000 is documented for copper and freshwater stoneflies (*Pteronarcys californica*; USEPA 1980), but the reasons for this phenomenon are unknown. The high tolerance to copper and other metals of mayfly larvae (*Baetis thermcius*), and high copper accumulations, is attributed, in part, to the selective induction of metal binding proteins in the gut (Sumi et al. 1991; Table 3). Marine amphipods readily accumulate dissolved copper from seawater in a dose-dependent manner (Weeks and Rainbow 1991). But some species of talitrad amphipods are unable to meet their copper requirements from seawater alone and depend on dietary sources of copper (Weeks and Rainbow 1993). Mesocosm studies with freshwater zooplankton assemblages show that increasing copper

concentrations in the range 0 to 50 µg/L causes a reduction in total zooplankton and changes in diversity; within 4 days, copepods became dominant at the expense of cladocerans (Havens 1994).

Soldier crabs (*Mictyris longicarpus*) accumulate copper mostly from sediments rather than the water column (Weimin et al. 1994). The fine particles of sediment trapped as food contain bioavailable fractions of copper and other metals, and these significantly correlate with metal concentrations in the body of the crab. However, copper accumulation from sediments by soldier crabs occurred only at an artificially high concentration (1,900 mg Cu/kg DW sediment), which also had toxic effects. Soldier crabs seem unable to regulate copper within their bodies (Weimin et al. 1994).

In shore crabs (*Carcinus maenas*), several days of exposure to sublethal concentrations of waterborne copper cause extensive damage to gill epithelium; at lethal concentrations, tissue hypoxia is probably the major effect of copper (Nonnotte et al. 1993). Starved shore crabs show a reduction in carapace copper concentrations and heavier midgut glands; starvation in combination with copper exposure (500 µg/L) results in an increase in copper in the carapace and a decrease in carapace calcium (Scott-Fordsmand and Depledge 1993). Shore crabs in seawater with high (10 mg/L) levels of waterborne copper show reductions in hemolymph sodium, gill sodium-potassium-ATPase activity, activities of various midgut gland enzymes (hexokinase, phosphofructokinase, pyruvate kinase), and hemolymph electrolytes (Hansen et al. 1992a, 1992b).

In the rusty crayfish (*Orconectes rusticus*), toxicity of copper at high concentrations is due to the coagulatory action on cellular proteins and to interference with respiratory processes; at low concentrations, copper causes degenerative changes in certain tissues and interferes with glutathione equilibrium (Hubschman 1967). Larvae of the red crayfish (*Procambarus clarkii*) exposed to copper as embryos are less sensitive than those exposed after hatching, suggesting acclimatization (Rice and Harrison 1983).

Annelids

Aquatic oligochaetes (*Lumbriculus variegatus*) do not accumulate significant amounts of copper when compared to controls after exposure for 30 days in sediments containing as much as 90.1 mg Cu/kg DW or in water containing as much as 2.3 µg Cu/L (Ankley et al. 1994). Larvae of the sandworm (*Nereis diversicolor*) are more resistant to copper with increasing organism age and with increasing temperature and salinity of the medium (Ozoh and Jones 1990). In adult sandworms, whole body loadings of copper usually increase with increasing temperature in the range of 12-22° C and with decreasing salinity in the range 0.7-3.1% (Ozoh 1992b); however, copper-temperature-salinity interactions are significant and complex in this species (Ozoh 1994).

Fishes

Adverse sublethal effects of copper on behavior, growth, migration, and metabolism occur in representative species of fishes at nominal water concentrations between 4 and 10 µg/L. In sensitive species of teleosts, copper adversely affects reproduction and survival from 10-20 µg Cu/L (Hodson et al. 1979; Table 5). Copper exerts a wide range of physiological effects in fishes, including increased metallothionein synthesis in hepatocytes, altered blood chemistry, and histopathology of gills and skin (Iger et al. 1994). At environmentally realistic concentrations, free copper adversely affects resistance of fishes to bacterial diseases; disrupts migration (that is, fishes avoid copper-contaminated spawning grounds); alters locomotion through hyperactivity; impairs respiration; disrupts osmoregulation through inhibition of gill Na^+-K^+-activated AT-Pase; is associated with tissue structure and pathology of kidneys, liver, gills, and other hematopoietic tissues; impacts mechanoreceptors of lateral line canals; impairs functions of olfactory organs and brain; and is associated with changes in blood chemistry, enzyme activities, and corticosteroid metabolism (Hodson et al. 1979). Copper-induced cellular changes or lesions occur in kidneys, lateral line, and livers of several species of marine fishes (Gardner and LaRoche 1973).

Copper-induced mortality in teleosts is reduced in waters with high concentrations of organic sequestering agents and in genetically resistant species (Hodson et al. 1979). At pH values less than 4.9 (that is, at pH values associated with increased aluminum solubility and toxicity), copper may contribute to the demise of acid-sensitive fishes (Hickie et al. 1993). Copper affects plasma Na^+ and gill phospholipid activity; these effects are modified by water temperature and hardness (Hansen et al. 1993). In red drum, copper toxicity is higher at comparatively elevated temperatures and reduced salinities (Peppard et al. 1991). Copper is acutely toxic to freshwater teleosts in soft water at concentrations between 10 and 20 µg/L (NAS 1977). In rainbow trout, copper toxicity is markedly lower at high salinities (Wilson and Taylor 1993). Comparatively elevated temperatures and copper loadings in the medium cause locomotor disorientation of tested species (Kleerekoper 1973). Copper may affect reproductive success of fish through disruption of hatch coordination with food availability or through adverse effects on larval fishes (Ellenberger et al. 1994). Chronic exposure of representative species of teleosts to low concentrations (5 to 40 µg/L) of copper in water containing low concentrations of organic materials adversely affects survival, growth, and spawning; this range is 66 to 120 µg Cu/L when test waters contain enriched loadings of organic materials (Hodson et al. 1979).

Larval and early juvenile stages of eight species of freshwater fishes are more sensitive to copper than embryos

(McKim et al. 1978) or adults (Hodson et al. 1979). But larvae of topsmelt (*Atherinops affinis*) are increasingly sensitive to copper with increasing age. Topsmelt sensitivity is associated with increasing respiratory surface area and increasing cutaneous and branchial uptake of copper (McNulty et al. 1994).

Sublethal exposure of fishes to copper suppresses resistance to viral and bacterial pathogens (Rougier et al. 1994) and, in the case of the air-breathing catfish (*Saccobranchus fossilis*), affects humoral and cell-mediated immunity, the skin, and respiratory surfaces (Khangarot and Tripathi 1991). Rainbow trout exposed to 50 µg Cu/L for 24 h—a sublethal concentration—show degeneration of olfactory receptors that may cause difficulties in olfactory-mediated behaviors such as migration (Klima and Applehans 1990). The primary site of sublethal copper toxicity in rainbow trout is the ion transport system of the gills (Hansen et al. 1993). In European sea bass (*Dicentrarchus labrax*), copper compromises the defense system of red blood cells against active forms of oxygen, leading to increased membrane lipid peroxidation (Roche and Boge 1993).

Dietary copper is more important than waterborne copper in reducing survival and growth of larvae of rainbow trout (Woodward et al. 1994). Simultaneous exposure of rainbow trout to dietary and waterborne copper results in significant copper assimilation. Diet is the main source of tissue copper; however, the contribution of waterborne copper to tissue burdens increases as water concentrations rise (Miller et al. 1993).

Rate and extent of copper accumulations in fish tissues are extremely variable between species and are further modified by abiotic and biological variables. Copper accumulations in fish gills increase with increasing concentrations of free copper in solution, increasing dissolved organic carbon (DOC), and decreasing pH and alkalinity (Playle et al. 1993a, 1993b). Starved Mozambique tilapia accumulate significantly more copper from the medium in 96 h than did tilapia fed a diet containing 5.9 mg Cu/kg DW ration (Pelgrom et al. 1994). The bioconcentration factor for whole larvae of the fathead minnow was 290 after exposure for 30 h, but only 0.1 in muscle of bluegills after 660 h (USEPA 1980). Prior exposure of brown bullheads (*Ictalurus nebulosus*) to sublethal copper concentrations for 20 days before exposure to lethal copper concentrations produces higher copper concentrations in tissues of dead bullheads than in those not previously exposed; however, the use of tissue residues is not an acceptable autopsy procedure for copper (Brungs et al. 1973). Rising copper concentrations in blood plasma of catfish (*Heteropneustes fossilis*) seem to reflect copper stress, although the catfish appear outwardly normal. Plasma copper concentrations of catfish increase from 290 µg Cu/L in controls at start to 380 µg Cu/L in survivors at 72 h (50% dead); a plasma copper concentration of 1,060 µg Cu/L at 6 h is associated with 50% mortality (Banerjee and Homechaudhuri 1990). In rainbow trout, copper is rapidly eliminated from plasma; the half-time persistence is 7 min for the short-lived component and 196 min for the long-lived component (Carbonell and Tarazona 1994).

Attraction to waters containing low (11 to 17 µg/L) concentrations of copper occurs in several species of freshwater teleosts, including goldfish (*Carassius auratus*) and green sunfish (*Lepomis cyanellus*); however, other species, including white suckers (*Catostomus commersonii*), avoid these waters (Kleerekoper 1973). In avoidance/attraction tests, juvenile rainbow trout avoided waters containing 70 µg Cu/L but were significantly attracted to water containing 4,560 µg Cu/L; a similar pattern was observed in tadpoles of the American toad, *Bufo americanus* (Birge et al. 1993). Copper concentrations in the range of 18 to 28 µg/L interfere with bluegill growth and prey choice (Sandheinrich and Atchison 1989). Copper interferes with the ability of fish to respond positively to L-alanine, an important constituent of prey odors; concentrations as low as 1 µg Cu/L inhibit this attraction response in some species (Steele et al. 1990).

Increased tolerance to copper was observed in fathead minnows after prolonged exposure to sublethal concentrations, but tolerance was not sustained on removal to clean water. Copper tolerance in fathead minnows is attributed to increased production of metallothioneins (Benson and Birge 1985). Copper tolerance in rainbow trout seems dependent on changes in sodium transport and permeability (Lauren and McDonald 1987a).

Integrated Studies

Bioconcentration and biomagnification of copper occurs in the food chain of diatom (*Skeletonema costatum*) to clam (*Donax cuneatus*) to white prawn (*Penaeus indicus*). All species accumulate copper from the medium, and clams and shrimp from the diet. Maximum concentrations after exposure to 200 µg Cu/L and diets for 10 days, in mg Cu/kg FW, are 2.8 in whole diatoms, 13.6 in clam soft parts, and 33.9 in whole shrimp (Rao and Govindarajan 1992). In the marine food chain of phytoplankton to clam (*Tellina tenuis*) to juvenile plaice (*Pleuronectes platessa*), copper accumulates in a concentration-dependent manner in viscera of plaice. All organisms held in 10, 30, or 100 µg Cu/L solutions for 100 days had reduced growth. Copper concentrations, in mg Cu/kg DW at day 100, in soft parts of clams (*T. tenuis*) were 270 in the 10 µg/L group, 470 in the 30 µg/L group, and 1,100 in the 100 µg/L group vs. less than 50 in the controls; for plaice viscera, these values were 30 in controls, 71 in the 10 µg/L group, 147 in the 30 µg/L group, and 467 mg/kg DW in the 100 µg/L group (Saward et al. 1975). Accumulations in Pacific oysters held in copper-loaded sediments are similar to those of oysters contaminated through ingestion of diatoms (*Haslea ostrearia*). However, accumulations are highest in Pacific

oysters when exposed through the medium (Ettajani et al. 1992); in that study, a concentration of 30 µg Cu/L medium for 21 days results in copper concentrations of 137 mg/kg DW in diatoms and 1,320 mg/kg DW in oyster soft parts. Oysters fed contaminated diatoms in the study had 419 mg Cu/kg DW soft parts. Oysters held in sediments containing 108 mg Cu/kg DW—a level reached after exposure for 21 days to 300 µg Cu/L—had 401 mg Cu/kg DW (Ettajani et al. 1992). Copper-induced changes in population density and community metabolism occur in an aquatic mesocosm of algae, protozoans, rotifers, oligochaetes, and bacteria; death of rotifers, algae, and oligochaetes occurs at concentrations as low as 700 µg Cu/L. Adverse effects occur at 300 to 700 µg Cu/L but are negated by increasing concentrations of dissolved organic matter (Sugiura et al. 1982).

Transfer of copper from wood treated with chromated copper arsenate (CCA) occurs in estuarine algae (*Ulva* sp., *Enteromorpha* sp.), American oysters, mud snails (*Nassarius obsoletus*), and fiddler crabs (*Uca* spp.; Weis and Weis 1992). Algae, barnacles, and mussels from CCA-treated lumber show elevated concentrations of copper when compared to reference sites. The epibiotic estuarine community that forms on CCA-treated wood has lower species richness, diversity, and biomass when compared to untreated lumber (Weis et al. 1993b). Copper is trophically transferred from CCA-exposed American oysters to predatory gastropods (*Thais* sp.), resulting in reduced gastropod feeding and growth (Weis and Weis 1993).

Birds

No data are available on the toxicity of copper to avian wildlife. All studies with birds and copper use domestic chickens, ducks, or turkeys (Table 6). Copper, however, may indirectly affect avian wildlife by curtailing certain prey species. Winger et al. (1984), for example, show that apple snails (*Pomacea paludosa*) are not only extremely susceptible to copper (LC50 of 24 to 57 µg/L in 96 h; immatures most sensitive), but are the primary food of the snail kite (*Rostrhamus sociabilis*), an endangered species. The decline of the apple snail in southern Florida coincided with the use of copper-diquat to control hydrilla aquatic weeds (*Hydrilla verticillata*), with serious implications for the snail kite (Winger et al. 1984).

In the domestic chicken, adverse effects of copper occur in chicks fed diets containing 350 mg Cu/kg ration for 25 days (reduced weight gain) and in adults given a dietary equivalent of more than 28 mg Cu/kg BW (Table 6). Chicks fed diets of 500 mg Cu/kg ration show damage to the gizzard lining; damage effects are attributed to the shedding of gizzard glandular cells into the keratin-like koilin layer, disrupting koilin production (Bremner 1979). Copper-induced gizzard histopathology in growing chicks is not reversed by zinc or vitamins B_{12} or E (Poupoulis and Jensen 1976). Supplementing chick diets with copper did not prove markedly advantageous (Poupoulis and Jensen 1976), provided that normal rations had about 4 mg Cu/kg and adequate iron (Carlton and Henderson 1964b). Unlike mammals, chicks fed copper-supplemented diets do not have elevated copper concentrations in liver or signs of liver damage (Bremner 1979). Broiler hens housed on slats made of lumber pressure-treated with chromated copper arsenate showed severe foot-pad dermatitis and excessive mortality after 17 weeks; however, arsenic and cresylic acid—not copper—may be the responsible agents (Sander et al. 1994).

Ducklings (*Anas* spp.), unlike chicks, accumulate copper in livers when fed diets supplemented with high loadings of copper (Wood and Worden 1973). Domesticated mallards show a dose-time dependent increase in copper liver concentrations, with a maximum concentration of 254 mg Cu/kg DW liver (Table 6). Mallards seem to prefer drinking water containing 100 mg Cu/L over distilled water (Table 6); however, these birds were molting and this may have influenced their response because trace mineral requirements rise during molting (Rowe and Prince 1983).

In turkeys, natural diets with as much as 800 mg Cu/kg ration have no adverse effects on growth or survival. But purified diets are toxic to turkeys in three weeks, and purified diets that contain as little as 50 mg Cu/kg ration produce adverse effects (Waibel et al. 1964). Turkeys fed purified diets with supplemented copper show a dose-dependent increase in mortality and decrease in growth; these effects are attributed to a copper-accelerated dietary deterioration (Supplee 1964). Turkey growth and survival are acceptable when fed purified diets supplemented with as much as 800 mg Cu/kg ration provided that effective levels of added antioxidant (0.02% ethoxyquin) and stabilized sources of vitamins A and D are present (Supplee 1964).

Mammals

Wilson's disease is the only naturally occurring neuropathological condition in humans and other mammals in which copper poisoning is implicated. People with Wilson's disease have severe pathological changes in the brain, especially in the basal ganglia, and in the liver; pathology is associated with excess copper in tissues (Doherty et al. 1969). Copper concentrations in tissues from children that die from Wilson's disease are as much as 2,217 mg/kg DW in liver and 1,245 mg/kg DW in kidney (Table 7). Long-term exposure of humans to copper dust irritates the nose, eyes, and mouth and causes headaches, dizziness, nausea, and diarrhea (USEPA 1980; ATSDR 1990). Drinking water that contains higher than normal concentrations of copper may cause vomiting, diarrhea, stomach cramps, nausea, and greenish or bluish stools and saliva. Intentionally high intakes of copper may result in liver and kidney damage, and sometimes death, especially in children. The seriousness of the effects of copper is expected to increase with increasing dose and duration of exposure (USEPA 1980;

ATSDR 1990). Human tissues exposed directly to copper or copper salts will suffer adverse effects because of copper absorption. This is the case for copper bracelets on sweaty skin, for certain intrauterine devices, and for copper dental fillings (USEPA 1980). In monkeys, copper used as dental fillings in deciduous teeth causes more severe pulp damage than did other materials studied (USEPA 1980).

Mammals and birds are 100-1,000 times more resistant to copper than other animals (Schroeder et al. 1966). But excessive dietary intakes of copper by 20- to 50-fold over normal levels may have serious effects in mammals. Depending on the species, growth and food intake may be reduced, anemia may develop, and liver, kidney, brain, and muscle may degenerate, often resulting in death (Bremner 1979; ATSDR 1990). Copper poisoning in mammals may result from consumption of plants treated with copper-containing pesticides, from the veterinary use of copper sulfate to control helminthiasis and infectious pododermatitis in cattle and sheep, and from the ingestion of contaminated soils and vegetation near copper mining and refining operations (NAS 1977). Emissions from copper mines and smelters are often associated with deaths of horses, cows, and sheep; pasture lands, in some cases, are fit for grazing only after heavy rains (Hutchinson 1979).

Ruminant mammals are significantly more sensitive to copper than nonruminant mammals and poultry (Schroeder et al. 1966; NAS 1977). Signs of copper poisoning in ruminants include vomiting, excessive salivation, abdominal pain, diarrhea with greenish-tinted feces, pathology of internal organs, elevated copper concentrations in liver, altered enzyme activities in liver and serum, and collapse and death within 24 to 48 h (NAS 1977). Young calves may develop copper toxicosis at relatively low copper intakes, especially when receiving milk-based diets; goats, however, seem resistant to copper toxicosis (Bremner 1979). Among ruminants, domestic sheep are particularly susceptible to copper insult from grazing on pastures treated with copper-containing fungicides and molluskicides or from inadvertently consuming diets specially formulated for pigs and which contain large amounts of copper as a swine growth stimulant (Todd 1969; Bremner 1979).

Chronic copper poisoning in domestic sheep is first characterized by a period of passive accumulation of copper in the tissues. This period varies from a few weeks to more than a year. During this time the animal appears outwardly normal although the liver may contain more than 1,000 mg Cu/kg DW and plasma activities of aspartate transaminase, sorbitol dehydrogenase, lactic dehydrogenase, and arginase increase, indicating that liver damage has occurred. During the last few weeks of the passive phase, and prior to the so-called toxic phase, liver histopathology of parenchymal cells and copper-containing Kupffer cells occurs. The toxic phase, which is an acute illness and referred to as the hemolytic crisis, usually results in death 2-4 days later. During this phase sheep refuse to eat but have an excessive thirst. The eyes are usually sunken. The venous blood is chocolate colored. The liver is jaundiced. The kidneys are completely gorged with hemoglobin breakdown products and the medulla and cortex are black. The spleen is enlarged, with the parenchyma a deep brown to black color. The onset of these signs in sheep is associated with liberation of copper from the liver and a massive increase in blood copper concentrations. The increased blood copper concentrations lead to an increase in blood methemoglobin and a sudden fall in the erythrocyte glutathione level immediately followed by massive hemolysis and kidney damage, leading to uremia and death. At the time of crisis, elevated serum creatine phosphokinase activity suggests that muscle cell membranes are affected, and elevated serum glutamic oxaloacetate transaminase (SGOT) and lactic dehydrogenase activities indicate progressive liver necrosis (Doherty et al. 1969; Todd 1969; Thompson and Todd 1974; Bremner 1979). It is emphasized that (1) blood copper status and liver function in sheep experimentally poisoned with copper sulfate are linked to elevated SGOT activities 1 to 6 weeks in advance of obvious external signs (MacPherson and Hemingway 1969); (2) copper chloride is 2 to 4 times more toxic to sheep than copper sulfate is (NAS 1977); and (3) the use of copper-enriched feeding stuffs increases the risk of chronic copper poisoning in sheep fed purified rations (Froslie et al. 1983). Also, sheep that accumulate higher than normal amounts of copper in the liver (i.e., 1,900 mg Cu/kg DW) are more severely affected by lupinosis (acute liver atrophy due to poisoning by ingestion of plants of *Lupinus* spp.) than sheep with normal (40 mg/kg DW) concentrations of copper in the liver (Gardiner 1967).

Copper toxicosis in lambs of domestic sheep occurs at dietary concentrations between 8 and 60 mg Cu/kg ration. The wide range of dietary concentrations is a function of copper availability. Availability, in turn, is influenced by dietary composition, genetic influence, age, breed, sex, physiological state, and interactions with other dietary constituents including iron, zinc, and molybdenum (Bremner 1979). Chronic copper poisoning in lambs occurs at dietary levels as low as 27 mg Cu/kg DW ration (Buckley and Tait 1981). During the passive phase, lambs—like adults—have normal plasma copper concentrations and seem outwardly unaffected. Unlike adults, copper accumulates in livers of lambs during a shorter period (several weeks to months vs. months to years). Signs of hemolytic crisis and death within a few days are similar for both adults and lambs. Elevated plasma aspartate aminotransferase (AAT) activity in lambs—up to 10 times higher than controls—occurs 4 to 8 weeks before the hemolytic crisis (Buckley and Tait 1981) and strongly indicates a need for more research on the usefulness of AAT and other enzymes as early indicators of copper stress. A recommended treatment for lambs diagnosed with chronic copper poisoning is 20 mL of a mixture

containing 100 mg of ammonium molybdate and 1 g of sodium sulfate administered orally 5 days weekly (Doherty et al. 1969).

In domestic pigs, copper toxicosis results from eating diets containing 250 mg Cu/kg ration and is characterized by anemia, jaundice, elevated levels of Cu in serum and liver, and elevated serum AAT activity (USEPA 1980). Shortly before death, copper-poisoned pigs had white noses, poor balance, stomach histopathology, orange cirrhotic livers, anorexia, and anemia (Higgins 1981).

In rodents, copper administered by single intraperitoneal or subcutaneous injection is lethal at 3 to 7 mg Cu/kg BW (Table 7). Mice died when their drinking water had 640 mg Cu/L (Table 7). In rats, copper accumulation in kidneys and lungs is similar regardless of route of administration (Romeu-Moreno et al. 1994). Concentrations of copper in serum of rats (*Rattus* sp.) reflect dietary copper; concentrations in liver and kidney are directly related to serum Cu and ceruloplasmin (Petering et al. 1977). As serum Cu concentrations rise in rats, levels fall for serum cholesterol, triglycerides, and phospholipids (Petering et al. 1977).

Proposed Criteria and Recommendations

Proposed copper criteria for the protection of agricultural crops, aquatic life, terrestrial invertebrates, poultry, laboratory white rats, livestock, and human health are summarized in Table 8.

Table 8. Proposed copper criteria for the protection of natural resources and human health.

Resource, criteria, and other variables	Effective copper concentration	Reference[a]
Agricultural Crops		
Irrigation water	<1.0 mg/L	1
Leaves		
Severe deficiency	<4 mg/kg dry weight (DW)	2
Deficient	<5 mg/kg DW	1, 3
Mild to moderate deficiency	4 to 5 mg/kg DW	1, 3
Deficiency rare	>6 mg/kg DW	2
Sewage sludge		
Europe, acidic soils	50 to 140 kg/ha	4
United States		
All agricultural lands	<1,000 mg/kg DW	5
Florida	<100 mg/kg DW	4
Illinois	<280 kg/ha	4
Maryland, Massachusetts	140 to 280 kg/ha[b]	4
Minnesota, Missouri	140 to 560 kg/ha[c]	4
New York		
Agricultural soils	<125 kg/ha	4
Forests	<280 kg/ha	4
Wisconsin, acidic soils	50 to 140 kg/ha	4
Soils		
Deficient	<10 mg/kg DW	6
Safe	<280 kg/ha[d]	7
M-3 extractable soil copper	<60 mg/kg DW	8
Canada		
Agricultural lands	<100 mg/kg DW	4
Acidic soils, Alberta	<200 mg/kg DW	4
Industrial and other lands	<300 mg/kg DW	4
Former Soviet Union, maximum allowable concentration	3 mg/kg DW when extracted with ammonium acetate buffer	4
The Netherlands		
Normal	50 mg/kg DW	4
Moderately contaminated	100 mg/kg DW	4
Requires remediation	>500 mg/kg DW	4
United States, New Jersey	<170 mg/kg DW	4
Aquatic life, fresh water		
Sediments		
Great Lakes		
Nonpolluted	<25 mg/kg DW	4
Moderately polluted	25 to 50 mg/kg DW	4
Heavily polluted	>50 mg/kg DW	4

Table 8. *Continued.*

Resource, criteria, and other variables	Effective copper concentration	Reference[a]
Reduced abundance of benthos	480 to 1,093 mg/kg DW	9
Toxic to benthos	>9,000 mg/kg DW	9
Tissue concentrations; rainbow trout, *Oncorhynchus mykiss*; ratio of zinc to copper in gill or operclula		
Normal	Ratio >1.5	10
Probably copper-poisoned	Ratio 0.5 to 1.5	10
Acute copper poisoning	Ratio <0.5	10
Water		
Safe. No adverse effects on rainbow trout exposed from fertilization through 4 days after hatching		
In soft or medium water	2 to 5 µg/L	11
In hard water	5 to 8 µg/L	11
Death or teratogenicity in eggs of sensitive species of fishes and amphibians	5 to 10 µg/L	11
United States		
Safe; total recoverable copper; 24 h average	<5.6 µg/L	12
Maximum allowable concentration at 50 mg $CaCO_3$/L	12 µg/L	12
Maximum allowable concentration at 100 mg $CaCO_3$/L	22 µg/L	12
Maximum allowable concentration at 200 mg $CaCO_3$/L	43 µg/L	12
Inhibits fish growth and ability of fish to discriminate prey	18 to 28 µg/L	13
The Netherlands; total recoverable copper; maximum allowable concentration	<50 µg/L	14
Aquatic life, marine		
Seawater		
Safe. Total recoverable copper, 24 h average	<4.0 µg/L; not to exceed 23 µg/L at any time	12
Safe. Maximum concentration	<5.0 µg/L	15
Sediments		
Avoidance by clams	>5 mg/kg DW	16
Clam burrowing ability inhibited (water concentrations of 113 to 120 µg Cu/L)	>15 mg/kg DW	16
Not polluted	<40 mg/kg DW	15
Moderately polluted	40 to 60 mg/kg DW	15
Very polluted	>60 mg/kg DW	15
Reduced species diversity; sensitive species absent	>200 mg/kg DW	17
Toxic to juvenile bivalve mollusks	>2,000 mg/kg DW	17
Terrestrial invertebrates		
Earthworms, whole; disrupted lysozyme activity in coelomic fluid and coelomocytes	>28.5 mg/kg DW	18
Isopod, *Porcellio scaber*; whole		
Deficiency	Unknown	19
Uncontaminated	<250 mg/kg DW	19
Low contamination	250 to 400 mg/kg DW	19
Medium contamination	400 to 600 mg/kg DW	19
High contamination	600 to 1,000 mg/kg DW	19
Very high contamination	>1,000 mg/kg DW	19
Poultry, diets		
Deficient	<8.7 mg/kg DW ration; some deaths at 0.7 to 1.5 mg/kg DW ration; high frequency of vascular rupture at 2.7 mg/kg DW ration	3, 20, 33
Safe	<200 mg/kg DW feed	17
Recommended for growing chickens	>4 mg/kg DW diet plus adequate iron	20
Laboratory white rat, *Rattus* sp.		
Minimal	3 to 6 mg/kg FW diet; 0.15-0.3 mg/kg body weight (BW) daily	5

Table 8. *Continued.*

Resource, criteria, and other variables	Effective copper concentration	Reference[a]
Adequate	10 mg/kg DW diet	21
Livestock		
All species except sheep; diet		
Deficient	<5 mg/kg DW	2
Minimal	>5 to <15 mg/kg DW	1
Adequate	20 to 30 mg/kg DW	2
Cattle, *Bos* sp.; liver, copper-poisoned	>150 mg/kg FW; >450 mg/kg DW	22
Sheep, *Ovis aries*		
Toxic	20 to 30 mg/kg DW diet	2
Pig, *Sus* sp.		
Diet		
Safe	3 to 5 mg/kg DW	5
United Kingdom, maximum	200 mg/kg DW[e]	23
Tissue concentrations		
Fatal anemia with jaundice and stomach ulcerations; kidney vs. liver	95 to 800 mg/kg DW vs. 1,300 to 2,600 mg/kg DW	23
Human health		
Air		
Montana	<0.26 µg/m³ for 8 h; <1.57 µg/m³ for 24 h	5
Massachusetts	<0.54 µg/m³ for 24 h	5
Connecticut, North Dakota	<2 µg/m³ for 8 h	5
Florida	<4 µg/m³ for 8 h	5
Nevada	<5 µg/m³ for 8 h	5
Virginia	<16 µg/m³ for 24 h	5
New York	<20 µg/m³ for 1 year	5
United States; workplace; 8 h daily		
Fumes	<0.1 to <0.2 mg/m³	5
Dusts and mists	<1.0 mg/m³	5
Total	<1.0 mg/m³	12
Daily intake, all sources		
Deficiency in children	<0.1 µg/kg BW	12
Infants, normal	14 to 80 µg/kg BW; 0.5 to 1.0 mg	12, 24, 25
Children, normal	40 to 100 µg/kg BW; 1 to 2 mg	12, 24, 25
Teenagers and adults, normal	28 to 40 µg/kg BW; 2 to 4 mg	5, 12, 24, 25
Adults, safe and adequate	2 to 3 mg	5
Adults, toxic	15 mg in single dose	12
Diet		
Australia		
Seafood	<30 mg/kg FW	30
Shellfish; soft parts	<70 mg/kg FW; <266 mg/kg DW	27, 28
Fish muscle	<15 mg/kg FW	31
Malaysia; bivalve mollusks; soft parts	<30 mg/kg FW	29
Spain, total diet	<20 mg/kg DW	32
Drinking water		
United States, safe	<1.0 mg/L (exceeded by about 1% of all samples)	12
Kansas, Rhode Island	<1.0 mg/L	5
Minnesota	<1.3 mg/L	5
Proposed, United States	<1.3 mg/L	5
Satisfactory smell and taste	<1.0 to 1.3 mg/L	5, 12
Associated with diarrhea, abdominal cramps, and nausea	>1.3 mg/L	26
Health advisory for children and adults	Not to exceed 1.3 mg/L for more than 1 day	5
Adverse taste	>1.5 mg/L	12
Fish and shellfish collection locales; marine	<4 µg/L	27
Tissues; human		
Blood; deficient vs. adequate	<0.8 mg/L vs. 1.03 mg/L	12
Serum; normal vs. toxic	1.64 mg/L vs. 2.86 mg/L	12

[a]1,NAS 1977; 2, Gupta 1979; 3, Carlton and Henderson 1963; 4, Beyer 1990; 5, ATSDR 1990; 6, King et al. 1984; 7, Reed et al. 1993; 8, Alva et al. 1995; 9, Mackenthun and Cooley 1952; 10, Carbonell and Tarazona 1993; 11, Birge and Black 1979; 12, USEPA 1980; 13, Sandheinrich and Atchison 1989; 14, Enserink et al. 1991; 15, Fagioli et al. 1994; 16, Roper and Hickey 1994; 17, Bryan and Langston 1992; 18, Goven et al. 1994; 19, Hopkin et al. 1993; 20; Carlton and Henderson 1964b; 21, Dodds-Smith et al. 1992a; 22,

Table 8. *Continued.*

Gummow et al. 1991; 23, Higgins 1981; 24, Aaseth and Norseth 1986; 25, Schroeder et al. 1966; 26, Knobeloch et al. 1994; 27, Talbot et al. 1985; 28, Brown and McPherson 1992; 29, Mat 1994; 30, Greig and Sennefelder 1985; 31, Mathews 1994; 32, Daramola and Oladimeji 1989; 33, Carlton and Henderson 1964a.
[b]Soil cation exchange capacity less than 5 meq/100 g for 140 kg/ha and more than 5 meq/100 g for 280 kg/ha.
[c]Soil cation exchange capacity ranges from less than 5 to more than 15 meq/100 g.
[d]Higher levels of 365 kg Cu/ha had no effect on corn yield or copper content in corn.
[e]Diet should also contain 150 mg Zn/kg and 200 mg Fe/kg to further reduce the chances of copper toxicity to pigs.

Copper is essential to normal plant growth, and copper deficiency is known in various agricultural crops such as vegetables and grains (Gupta 1979). Crops seem to be protected against copper deficiency when growing soils contain greater than 10 mg Cu/kg DW and leaves greater than 6 mg Cu/kg DW (Table 8). With some exceptions, agricultural crops are protected against copper toxicosis when irrigation waters contain less than 1.0 mg Cu/L and soils less than 170 mg Cu/kg DW (Table 8). But adverse effects occur on root development of seedling pines at irrigation water concentrations as low as 200 µg Cu/L (Arduini et al. 1995) and on growth of citrus trees when extractable copper in the soil exceeds 60 mg/kg DW (Alva et al. 1995). States allow application of sewage sludge to agricultural soils if total copper in the sludge does not exceed 1,000 mg/kg DW (100 mg/kg DW in Florida), or if the application rate for sludge does not exceed 280 kg sewage sludge per surface acre (50 kg/ha in Wisconsin; Table 8). The practice by some localities of applying raw sewage sludge to crop soils on the basis of kg sludge/surface acre ratio should be discouraged unless the sludge is periodically analyzed for copper and other contaminants.

Proposed criteria to protect most species of freshwater aquatic life from copper toxicity or deficiency include maximum water concentrations over a 24-h period of 12 µg Cu/L in soft water and 43 µg/L in hard water, sediment concentrations less than 480 mg Cu/kg DW, and, in rainbow trout, a zinc/copper ratio in gill or opercle greater than 1.5 (Table 8). However, the proposed maximum water concentration range of 12-43 µg Cu/L exceeds the 5-10 µg/L range that is lethal or teratogenic to sensitive species of fishes and amphibians (Birge and Black 1979) and overlaps the 18-28 µg/L range that inhibits growth and ability to discriminate prey for other species (Sandheinrich and Atchison 1989). Some scientists state that laboratory studies tend to overestimate the adverse effects of copper on freshwater abundance and diversity and suggest more research on field mesocosms receiving water directly from the system under investigation (Clements et al. 1990). In marine ecosystems, copper concentrations should not exceed 23 µg Cu/L at any time, and sediments should contain less than 200 mg Cu/kg DW (Table 8). But adverse sublethal effects of copper to representative species of estuarine algae, mollusks, and arthropods frequently occur at less than 10 µg Cu/L (Bryan and Langston 1992). Also, extrapolation of laboratory data on copper and marine benthos to actual field conditions is difficult because of changing environmental conditions such as thermosaline regimes and the nature of the sediment substrate (Ozoh 1992c).

Among sensitive species of terrestrial invertebrates, earthworms show disrupted enzyme activities at whole body concentrations as low as 28.5 mg Cu/kg DW (Table 8). Soil copper concentrations between 53 and 100 mg/kg DW kill soil nematodes and soil faunal communities (Parmelee et al. 1993; Donkin and Dusenbery 1993) and cause a reduction in cocoon production of earthworms (Ma 1984; Spurgeon et al. 1994). Diets that contain between 50 and 63 mg Cu/kg ration inhibit development and reproduction in gypsy moths and oribatid mites (Denneman and van Straalen 1991; Gintenreiter et al. 1993). The wood louse (*Porcellio scaber*), an isopod, is proposed as a bioindicator of copper contamination in terrestrial ecosystems because whole body concentrations seem to reflect copper loadings in the isopod's immediate environment (Hopkin et al. 1993; Table 8). More research is recommended on isopods and other sentinel organisms.

Quantitative data are missing on copper effects on avian and mammalian wildlife, and this represents a high priority research need. Some data are available for copper and poultry and livestock, but extrapolation of these results to wildlife species is contraindicated in view of the wide range in sensitivities to copper between species. Domestic chickens show good growth and survival when their diets contain adequate iron and more than 4 and less than 200 mg Cu/kg ration (Carlton and Henderson 1964b). In sheep—and some other mammals—prior knowledge of copper stress would allow adequate time for treatment (i.e., prophylactic dosing with ammonium molybdate plus sodium sulfate or intravenous injection of chelating agents) to prevent sudden death during copper-induced hemolytic crisis (MacPherson and Hemingway 1969). In sheep, for example, elevated SGOT activity is an early indicator of copper poisoning and is measurable 1 to 6 weeks before the hemolytic crisis stage (MacPherson and Hemingway 1969).

Providing prophylactic licks containing zinc sulfate and sulfur to African cattle, buffaloes, and impalas seems to be successful in protecting against the lethal effects of excess airborne copper in the grazing area (Gummow et al. 1991).

The proposed domestic drinking water criterion of less than 1.0 mg Cu/L for the protection of human health is not based on copper toxicosis but on the unpleasant taste which develops with higher levels of copper in drinking water (USEPA 1980). Increased copper levels (>1.3 mg Cu/L) in household water supplies caused by corrosion of copper plumbing materials may adversely affect infants and young children among residents of newly constructed or renovated homes (Knobeloch et al. 1994). Human groups at greatest risk to copper toxicosis now include young children subjected to unusually high concentrations of copper in soft or treated water held in copper pipes or vessels, medical patients with Wilson's disease, medical patients treated with copper-contaminated fluids in dialysis or parenteral administration, people with a glucose-6-phosphate dehydrogenase (G-6-PD) deficiency (about 13% of the Afro-American male population has a G-6-PD deficiency) who drink water containing greater than 1.0 mg Cu/L, and occupationally exposed workers (USEPA 1980).

Other copper research areas that seem to merit additional effort include (1) establishment of specific biomarkers for copper toxicity (ATSDR 1990); (2) development of a national system to verify incidents of deficiency and excess of copper and interrelated trace elements in species of concern (NAS 1977); (3) clarification of copper interactions with molybdenum, sulfate, iron, and zinc in plant and animal metabolisms (NAS 1977; Eisler 1989, 1993); (4) the role of copper in carcinogenesis, mutagenesis, and teratogenesis (NAS 1977; ATSDR 1990) because preliminary evidence suggests that exposure to grossly elevated concentrations of copper produces teratogenicity in fish (Birge and Black 1979) and mammals (Aaseth and Norseth 1986), carcinogenicity in rodents (USEPA 1980; ATSDR 1990; Toussaint and Nederbragt 1993), and mutagenicity in rodents (ATSDR 1990), sheep (Bires et al. 1993), and grasshoppers (Bhunya and Behura 1986); (5) mechanisms by which copper deficiency results in neutropenia, with emphasis on the process of cellular differentiation and the viability of neutrophils in blood and marrow (Percival 1995); (6) copper status effects on resistance to endotoxin-induced injuries because burn and trauma patients show moderate copper deficiency and high risk to sepsis, and copper deficient rats are sensitive to endotoxins causing sepsis (DiSilvestro et al. 1995); (7) the role of aquatic organisms in copper cycling in aquatic ecosystems (Stokes 1979); (8) mechanisms of copper tolerance or acclimatization to high doses of copper (ATSDR 1990); (9) the relation between copper toxicosis, copper absorption rates, and copper retention (Stokes 1979; ATSDR 1990); (10) effects on reproduction, neurotoxicity, and immune response (ATSDR 1990); (11) biochemistry and physiology of copper proteins (NAS 1977); (12) measurement of flux rates of ionic copper from metallic copper (ATSDR 1990); and (13) determination of safe levels of copper in livestock and poultry feeds (NAS 1977), and in diets of avian and mammalian wildlife.

Conclusions

Copper discharges to the global biosphere are due primarily to human activities, especially from the mining, smelting, and refining of copper and from the treatment and recycling of municipal and industrial wastes. Some copper compounds, especially copper sulfate, also contribute to environmental copper burdens because they are widely and intensively used in confined geographic areas to control nuisance species of aquatic plants and invertebrates, diseases of terrestrial crop plants, and ectoparasites of fish and livestock.

Copper concentrations in field collections of abiotic materials and living organisms are usually elevated in the vicinity of human activities and intensive copper use. Maximum copper concentrations recorded in selected abiotic materials are 5 $\mu g/m^3$ in air, 5 µg/L in groundwater, 12 µg/L in rainwater, 1,200 mg/kg DW in poultry litter, 7,000 mg/kg DW in soils, and 7,700 mg/kg DW in sewage sludge. In terrestrial vegetation, copper is usually less than 35 mg/kg DW except near smelters where it may approach 700 mg/kg DW and in certain copper-accumulator plants that may normally contain as much as 13,700 mg/kg DW. Aquatic vegetation from copper-contaminated sites contain as much as 1,350 mg Cu/kg DW vs. 36 mg/kg DW in conspecifics from reference sites. Terrestrial invertebrates from industrialized areas may contain from 137 to 408 mg Cu/kg DW whole organism. Aquatic invertebrates seldom contain as much as 95 mg Cu/kg DW, regardless of collection locale; exceptions include whole amphipods and lobster hepatopancreas (335-340 mg/kg DW) from copper-contaminated sites and many species of mollusks that normally contain 1,100-6,500 mg Cu/kg DW. Data are scarce on copper concentrations in field populations of amphibians and reptiles: crocodile eggs may contain as much as 60 mg Cu/kg DW and livers of some toads may contain as much as 2,100 mg Cu/kg DW without apparent adverse effects. Maximum copper concentrations in tissues of fishes, elasmobranchs, birds, and marine mammals from all collection sites are low when compared to more primitive organisms and never exceed 53 mg Cu/kg DW except liver (146-367 mg/kg DW); an exception is liver from endangered manatees (1,200 mg/kg DW) collected at a site treated with a copper-containing herbicide. Maximum copper concentrations in all tissues of terrestrial mammals, regardless of collection locale, are low and seldom exceed 29 mg/kg DW except kidneys (108 mg/kg DW) and livers (1,078 mg/kg DW) from animals near a copper refinery.

Copper deficiency is not a major public health concern in the United States, although skeletal deformities and leg fractures may occur in some copper-deficient children. Copper deficiency effects occur, however, in various species of terrestrial plants (reduced growth, necrosis, reduction in number of pollen grains, death), chickens (poor growth, high frequency of cardiovascular and skeletal lesions, low survival), turkeys (sudden death), rats (defective hemoglobin synthesis, lesions of the central nervous system, low survival, altered blood and liver enzyme activities), guinea pigs (lesions of the central nervous system), dogs (leg fractures), sheep and other ruminant mammals (sudden death, skeletal deformities), pigs (poor growth, decreased hemoglobin and erythrocytes, skeletal deformities), mink (reduced survival), and camels (anemia, emaciation, falling, fractures, death). Data are scarce or missing on copper deficiency effects in aquatic flora and fauna and in avian and terrestrial mammalian wildlife; additional studies of copper deficiency in these groups are merited. In sensitive terrestrial agricultural crops, copper deficiency occurs at less than 1.6 mg dissolved Cu/kg DW soil and less than 5 mg total Cu/kg DW leaves. For domestic chickens, copper deficiency occurs when chickens are fed diets containing less than 2.7 mg Cu/kg ration. Male weanling rats show deficiency effects when fed diets containing 0.13 mg Cu/kg ration vs. a copper-normal diet of 5.7 mg Cu/kg ration; earliest signs of copper deficiency in rats include low concentrations of copper in livers (less than 3.0 mg/kg DW vs. 12.6-15.0 mg/kg DW in controls), reductions in activities of cytochrome oxidase and succinoxidase, and prolonged sleeping times. Ewes of bactrian camels fed copper-deficient diets of less than 2.5 mg Cu/kg DW ration (vs. normal diet of about 11.0 mg Cu/kg DW) produce a high frequency of swaybacked lambs. Copper deficiency in mink is produced at daily intake rates equivalent to 3.5 mg Cu/kg BW for 50 weeks. Swine require high intakes of copper to avoid deficiency; daily intakes of less than 36 mg Cu/kg BW are associated with reductions in growth rate, hemoglobin, and hematocrit.

Copper and its compounds are not carcinogenic, mutagenic, or teratogenic at environmentally realistic concentrations. But under controlled conditions of grossly elevated exposures some studies suggest that copper is a potential carcinogen in rodents; mutagen in rodents, sheep, and grasshoppers; and teratogen in fish and small laboratory animals. More research is needed in this area.

Bioavailability and toxicity of copper to aquatic organisms depends on the total concentration of copper and its speciation. Both availability and toxicity are significantly reduced by increased loadings of suspended solids and natural organic chelators and increased water hardness. Toxicity to aquatic life is related primarily to the dissolved cupric ion (Cu^{+2}) and possibly to some hydroxyl complexes. Cupric copper (Cu^{+2}) is the most readily available and toxic inorganic species of copper in fresh water, seawater, and sediment interstitial waters. Cupric ion accounts for about 1% of the total dissolved copper in seawater and less than 1% in fresh water. In fresh water, cupric copper and some copper hydroxyl species are correlated with high toxicity to aquatic life, although carbonato species are much less toxic than other copper complexes. More research seems needed on the adsorption characteristics of most cupric ion complexes. In solution, copper interacts with numerous inorganic and organic compounds resulting in altered bioavailability and toxicity. Acknowledgment of these interactions is essential to the understanding of copper toxicokinetics. In aquatic invertebrates, copper disrupts gill epithelium at high concentrations and in fishes it interferes with osmoregulation; death is caused by tissue hypoxia associated with disrupted ATP synthesis. Copper detoxifying mechanisms in fishes include the induction of metallothioneins, allowing copper retention for weeks or months after absorption without toxicity. In higher vertebrates, excess copper is cytotoxic and alters protein configuration and lipid peroxidation rates. Mechanisms implicated in copper poisoning of mammals include free radical production, alteration in activities of several enzymes, and inhibited metallothionein synthesis. In mammals, copper is normally excreted via the bile in association with glutathione or unidentified high molecular weight proteins.

Excess copper is toxic to representative species of plants and animals. Significant adverse effects in terrestrial plants occur at concentrations as low as 40 µg Cu/L of nutrient solution, more than 10 mg Cu/kg DW in leaves, and greater than 60 mg extractable Cu/kg DW of soil. Sensitive species of terrestrial invertebrates show a reduction in growth, survival, or reproduction at more than 50 mg Cu/kg diet or 53-70 mg Cu/kg DW of soil. Many species of freshwater plants and animals die within 96 h at waterborne copper concentrations of 5.0-9.8 µg Cu/L, and sensitive species of freshwater mollusks, crustaceans, and fishes die at 0.23-0.91 µg Cu/L within 96 h. The most sensitive tested species of marine mollusks, crustaceans, and fishes have an LC50 (96 h) range from 28-39 µg Cu/L; significant sublethal effects to representative species of estuarine algae, mollusks, and arthropods frequently occur at 1-10 µg Cu/L. Mammals and birds are at least 100 times more resistant to copper than other organisms, but ruminant mammals are significantly more sensitive to copper than nonruminant animals and poultry. Excessive dietary intakes of copper by 20- to 50-fold over normal levels may, however, have serious adverse effects on birds and mammals. No data are available on copper toxicity to avian wildlife. Studies with poultry demonstrate that copper accumulates in livers at dietary concentrations as low as 15 mg Cu/kg DW ration, inhibits growth at 120 mg Cu/kg DW ration, and causes gizzard histopathology at 250 mg Cu/kg DW ration. Copper is lethal to representative species of mammals through a variety of routes: single oral doses of 6 to 637 mg Cu/kg BW in humans and 200 mg/kg BW in cattle or diets with more

than 80 mg Cu/kg ration (about 5.1 to 10.7 mg Cu/kg BW daily) fed to sheep or more than 238 mg/kg ration (more than 133 mg/kg BW daily) fed to rats. Adverse sublethal effects of copper to sensitive mammals occur in human infants at drinking water concentrations greater than 3 mg/L, in cattle at more than 4.2 mg/kg BW by way of drinking water or more than 20 mg/kg BW via diet, in sheep given daily oral doses of 7.5 to 15.0 mg/kg BW or fed diets containing more than 37.3 mg/kg ration, in rats given more than 7.9 mg/kg BW daily by way of diet (equivalent to more than 100 mg/kg DW ration), and in pigs at more than 14.5 mg/kg BW daily via diet.

Numerous and disparate copper criteria are proposed for protecting the health of agricultural crops, aquatic life, terrestrial invertebrates, poultry, laboratory white rats, and humans (Table 8); however, no copper criteria are now available for protection of avian and mammalian wildlife, and this needs to be rectified. Several of the proposed criteria do not adequately protect sensitive species of plants and animals and need to be reexamined. Other research areas that merit additional effort include biomarkers of early copper stress; copper interactions with interrelated trace elements in cases of deficiency and excess; copper status effects on disease resistance, cancer, mutagenicity, and birth defects; mechanisms of copper tolerance or acclimatization; and chemical speciation of copper, including measurement of flux rates of ionic copper from metallic copper.

Acknowledgments

I thank L. J. Garrett and P. W. Manning for library services; W. J. Birge, C. Hogstrand, O. H. Pattee, D. W. Sparling, and J. S. Weis for scientific and technical reviews of the manuscript; D. S. McGrath and B. A. Vairin for editorial services; and S. M. Lauritzen for layout.

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REPORT DOCUMENTATION PAGE

Form approved
OMB No. 0704-0188

1. AGENCY USE ONLY (Leave Blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	January 1998	Final

4. TITLE AND SUBTITLE

Copper Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review

5. FUNDING NUMBERS

6. AUTHOR(S)

R. Eisler

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESSES

U.S. Department of the Interior
U.S. Geological Survey/Biological Resources Division
Patuxent Wildlife Research Center
Laurel, Maryland 20708

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESSES

U.S. Department of the Interior
U.S. Geological Survey/Biological Resources Division
Washington, D.C. 20240

10. SPONSORING, MONITORING AGENCY REPORT NUMBER

Biological Science Report
USGS/BRD/BSR--1997-0002

11. SUPPLEMENTARY NOTES

Internally numbered as Contaminant Hazard Review Report 33

12a. DISTRIBUTION/AVAILABILITY STATEMENT

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13. ABSTRACT (Maximum 200 words)

Selective review and synthesis of the technical literature on copper and copper salts in the environment and their effects primarily on fishes, birds, mammals, terrestrial and aquatic invertebrates, and other natural resources. The subtopics include copper sources and uses; chemical and biochemical properties; concentrations of copper in field collections of abiotic materials and living organisms; effects of copper deficiency; lethal and sublethal effects on terrestrial plants and invertebrates, aquzatic organisms, birds, and mammals, including effects on survival, growth, reproduction, behavior, metabolism, carcinogenicity, mutagenicity, and teratogenicity; proposed criteria for the protection of human health and sensitive natural resources; and recommendations for additional research.

14. SUBJECT TERMS (Keywords)

Copper, copper sulfate, metals, toxicity, deficiency, criteria, residues, agriculture, nutrition, metallothionein, fish, invertebrates, amphibians, birds, wildlife, livestock, endangered species

15. NUMBER OF PAGES

iv + 98 pp

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	

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