FINAL REPORT

ICA PROJECT NO. 223

THE BIOLOGICAL IMPORTANCE OF COPPER

A Literature Review
June, 1993

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Preface

In 1973 the International Copper Research Association Incorporated initiated a grant to review the literature dealing with the biological importance of copper in marine and estuarine environments. This was followed by a second review in 1978. It was then apparent that a very large number of publications concerning copper in the marine environment were appearing each year and that an annual review was appropriate.

Reviews prior to 1984 considered copper only in marine and estuarine environments. However, events occurring on land and in freshwater were often mentioned because chemical and biological factors and processes pertinent to one environment could often be applied to the others. As a result, the review became larger, covering not only freshwater, saltwater and terrestrial environments but also agriculture and medicine. It was apparent from the literature that most of the general concepts about the importance and the effects of copper could be applied in all environments. This also meant that an understanding of the environmental chemistry of copper could be applied in medicine as well as agriculture, the marine environment as well as soils. The reviews pointed out the broad application of concepts about the biological importance as well as the environmental chemistry of copper.

The present review includes literature for the period 1992-1993. A number of earlierworks are included and a few appearing early in 1994 have been used. Often, the earlier references are from eastern Europe and Asia and only recently were included in the North American reference bases. References were obtained through literature search programs available through the Woodward Biomedical Library at The University of British Columbia. The metals section of the Marine Pollution Research Titles has been used as a source of European as well as North American References.

The review was written using 3,657 references selected from the literature searches. These references have been catalogued with those used in previous reviews to form the ICA Reference Collection which now includes 36,548 references. The collection is accessible to individuals in industry, government and academia. Key words, titles and authors can be searched with an AWK-based program for references that may be of interest. For information or requests contact A.G. Lewis, Dept. of Oceanography, The University of British Columbia, 6270 University Blvd., Vancouver, British Columbia, Canada, V6T 1Z4. FAX (604) 882-6091.

It will be apparent to the reader that the background of the reviewer (A.G.L.) is in marine sciences. With this in mind, special effort has been made to cover other areas. Because of the problems of obtaining certain references, particularly manuscript reports, this review should be considered as a "critical review" of the literature. The cross-referencing scheme used in the preparation and writing of the review provides an integration of concepts from all areas covered by the literature search. In many instances, pertinent references are listed under additional subheadings to provide the reader with specifics about the nature of the references. In essence, the references are grouped or discussed under five topics that form parts or all of the chapters in this review:

1. The benefits of copper to organisms and to humans.
2. What does copper do to organisms?
3. What are the sources of environmental copper?
4. What are the relationships between the chemistry of copper and its biological importance?
5. What chemical and geochemical changes occur to copper once it enters the environment?

In addition, a series of tables present environmental, tissue and food concentrations of copper selected from references used in the review. The collection of references and the preparation of much of this review was done by Leslie Chan, Dr. Brenda Harrison and Sharon De Wreede.

Signature of Grant Recipient:

A.G. Lewis, Professor
Department of Oceanography
The University of British Columbia

Executive Summary

Copper is required for the normal functioning of plants, animals and most microorganisms. In most cases, this is because copper is incorporated into a variety of organics that perform specific metabolic functions. One of the better known organometallic compounds is copper-zinc superoxide dismutase, a metalloenzyme that plays a key role in the enzymatic defense against oxygen toxicity. Prohaska and Failla (1993) comment that "... it is more difficult to think of a system that does not depend on copper than it is to list the numerous systems that do." Copper has been used by humans for medicinal purposes for thousands of years. The Egyptians and Chinese, for example, used copper salts therapeutically more than 2000 years ago. As a malleable metal with beneficial properties, copper is widely used by humans for domestic and industrial purposes.

Although copper is present in soils it is often not available for uptake by plants. Failure in the supply of adequate biologically available copper has the potential to produce copper deficiency and a variety of biochemical and physiological disorders in plants (e.g. Qin et al., 1992; Rao and Ownby, 1993; Smith and Vanden Berg, 1992a,b,c,d; Wilder and Strik, 1991). The application of information on copper in soils does not stop with a better understanding of plant growth. Adequate nutritition of domestic animals (e.g. Compère et al., 1993; Hendricksen et al., 1992) as well as wild animals (e.g. Dierenfeld, 1993) and humans is dependent upon a suitable source of copper and that, of course, means in forage crops or plants and animals used as food.

As copper is an essential metal, a physiological response can be produced by deficiency. As a toxicant at elevated levels of biologically available metal, a physiological response can be produced by an excess of copper. Most organisms operate somewhere between these two extremes, taking up the metal from the environment or food then storing or transferring it to sites of use. There is also evidence of hyperaccumulation of some metals by some plants as a defence mechanism against ingestion by herbivores (Boyd and Martens, 1992). Some of the uses of copper come from its ability to control the growth of organisms. This occurs when copper is biologically available and at concentrations that are detrimental. As a result, copper is used in a range of cidal agents.

The chemical nature of copper is very important in determining biological availability. Although evidence of this continues to accumulate, the potential detrimental impact of copper is still far too frequently inferred from levels of "total copper" or even the "presence" of copper. Pequegnat (1990) points out that "It is becoming increasingly difficult to convince some environmental regulators that the mere presence of a toxic chemical in marine sediments does not necessarily mean that it will adversely impact the biota". In an article entitled "Copper residues in the environment - what are we looking for?", Koldenhoven (1992) comments that "The fate of copper in the environment needs to be determined on the basis of which copper species are present and if those copper species are bioavailable".

When copper is introduced into a natural environment, or from one type of environment to another, the metal is exposed to different chemical conditions. This quite often leads to changes in metal speciation and changes in metal bioavailability. The amount of metal entering an environment and the chemical changes that occur are of importance in determining the fate of the metal as well as its biological impact. As a result, a number of studies have examined the flux of metals, including copper, as well as metal speciation (e.g. Report number 32 of the Joint Group of Experts on the Scientific Aspects of Marine Pollution (GESAMP)). Monitoring programs can also provide evidence of the level of anthropogenic input as well as some indication of the source of the metals. Areas of copper mineralization will have naturally elevated levels of soil or sediment copper; Runnells et al. (1992) point out that in aquatic situations like this, "... it may not be scientifically reasonable or technically possible to remediate the water to standards that are lower than the natural background concentrations". Wollast (1990) comments that information from surveys of the Rhone river provide evidence that "... trace metal concentrations in the Rhone are significantly lower than previous estimates and that although anthropogenic signals are present, the Rhone river is less polluted than expected". Diffuse sources of pollution have increased in importance with the strict controls on point source industrial discharges.

TABLE OF CONTENTS

I - THE BIOLOGICAL IMPORTANCE OF COPPER

I.1 INTRODUCTION

As an essential element, copper is required by organisms for a wide range of metabolic processes (e.g. Ebner, 1986; Kroker, 1991). Bakardjieva (1984) suggests that metal ions such as copper could even be considered as a prototype for the emergence of biologically important functional systems. As a malleable metal, copper is widely used by humans for domestic and industrial purposes. Since high levels of copper can be detrimental to organisms, it is very useful in the control of unwanted organisms. Thus, the metal plays many roles in microorganisms, plants, animals and humans. This review presents recent literature in lists of and discussions about the beneficial and detrimental roles that make copper biologically important.

Important recent reviews of the literature on copper deal with metals in soils, water, organisms, the effect of metal deficiencies and the anthropogenic effects of excess copper. With soils, these include reviews of concentrations in soils and plants of major areas of the world (e.g. Angelone and Bini, 1992; Chen, 1992b), the effects of deposition of metals in soils (e.g. Haygarth and Jones, 1992; Juste and Mench, 1992), attempts to model the chemistry of metals in soils (e.g. Harmsen, 1992) and the use of fungicides in plant disease control (Nene and Thapliyal, 1993). In water, major reviews deal with the chemistry of metals (e.g. Giusti et al., 1993) and numerical methods for water resources (Wood, 1993). Reviews of literature on copper in organisms include metal uptake and transport (Harris, 1993), the role of copper in immunity (Prohaska and Failla, 1993; Prohaska and Lukasewycz, 1990) and growth (e.g. Bowland, 1990) as well as the defects caused by dietary trace element deficiencies (Chesters and Arthur, 1988; Miniuk et al., 1991) or excesses (Spicer and Weber, 1991). In anthropogenic materials and effects, Henry and Harrison (1992) review literature on the fate of trace metals in sewage sludge compost, Gardner (1993) reviews literature on chemically-induced histopathology in aquatic invertebrates and Gadd (1993) the interactions of fungi with toxic metals and Gadd (1992) microbial control of heavy metal pollution. A number of these reviews appear in "Biogeochemistry of Trace Metals", edited by Adriano (1992). Broadscale reviews, such as the World Health Organization 1993 report "Our planet, our health" include limited discussions of metals in some sections.

I.2 - COPPER, AN ESSENTIAL METAL

The association of copper with organics, in organisms, produces a wide array of metabolic possibilities (e.g. Alfrey, 1992; Prohaska and Lukasewycz, 1990; Prohaska and Failla, 1993). It is found in a number of enzymes that play important roles in, for example, electron transport and antioxidant defense (Linder, 1991). Turnlund (1989) points out (page 21) that "While a Recommended Dietary Allowance has not been established for Cu (in humans), the estimated safe and adequate level of dietary Cu intake (ESADDI) for adults is 2 to 3 mg/d." In arriving at an evaluation of what this means in terms of dietary copper intake, she considers the problems of absorption and endogenous losses and suggests that the lower end of the RDA could be reduced to less than 1 mg/d. However, she points out (page 27) that "More research is needed with low levels of dietary Cu to acquire sufficient evidence on which to establish the dietary Cu requirement, the level below which Cu status cannot be maintained and Cu deficiency symptoms begin to appear." This would also be true for animals like the rat (RDA of 5 mg/kg dry matter; see for example Larsen, 1992) which are used as laboratory animal models of humans. It is also important to recognize the interactions that can occur between copper and other metals, particularly iron. In anemia associated with malnutrition, copper deficiency has been shown (laboratory animals) to reduce the absorption and metabolism of iron (Warrier et al., 1990).

Copper becomes biologically important either when it affects organisms or is used by humans. When considering the former, it is important to understand the concentration and biological availability of copper in soils. Effects on plants and plant composition has been related to soil chemical composition (e.g. Gorinova and Atanassov, 1993) although the numerous factors affecting bioavailability often make this a difficult task (e.g. Smithson et al., 1993). Although copper levels are often higher in soils that are rich in organics (e.g. Holmgren et al., 1993), the metal is complexed by the organics and, in many cases, not available for uptake by plants. Other factors can also affect the biological expression of copper -- metal-metal interactions for example. As a result of the numerous soil characteristics, it is necessary to consider metal desorption (e.g. Hogg et al., 1993), bioavailability and metal concentration when considering plant growth in various types of soils (e.g. Agrawal, 1992; Alva, 1992; Cuesta et al., 1993), or soil replacements (e.g. Handreck, 1993). Unfortunately, soil copper concentration rather than soil copper bioavailability is still used to estimate critical plant concentrations (e.g. Hole and Scaife, 1993). Failure in the supply of adequate biologically available copper has the potential to produce copper deficiency and a variety of biochemical and physiological disorders in plants (e.g. Qin et al., 1992; Rao and Ownby, 1993; Smith and Vanden Berg, 1992a,b,c,d; Wilder and Strik, 1991). It has also been related to the effect of diseases on plant crops (e.g. Evans et al., 1992a). Consideration of concentration and biological availability must also be made with soils receiving anthropogenic copper (e.g. Baccini and von Steiger, 1993). Although detrimental effects of excess copper have been shown, they are often incorrectly assumed on the basis of metal concentration rather than bioavailability. There is also evidence of hyperaccumulation of some metals by plants as a defence mechanism against ingestion by herbivores (Boyd and Martens, 1992).

The application of information on copper in soils does not stop with a better understanding of plant growth. Adequate nutritition of domestic animals (e.g. Compère et al., 1993; Hendricksen et al., 1992) as well as wild animals (e.g. Dierenfeld, 1993) and humans is dependent upon a suitable source of copper and that, of course, means in forage crops or food plants and animals. In dogs, for example, evidence presented by Czarnecki-Maulden et al. (1993) in an abstract caused the authors to suggest that "... the copper requirement of the dog is above the National Research Council (U.S.) recommendation of 0.8 mg bioavailable copper/1000 kcal ME". Copper deficiency in domestic grazing animals is a world-wide problem (Blincoe, 1993a; Haroun et al., 1992; Holmes, 1992) and the copper requirements of domestic animals have been examined by a number of authors (e.g. Blincoe, 1993b; Xin et al., 1993a). The effects of deficiencies vary, depending on the nature of the animal, the factors affecting metal concentrations and the level of any deficiency (Abdelrahman and Kincaid, 1992; Christensen, 1991; Graham and Keen, 1992; Stabel et al., 1993). Disease can be a mechanism that causes changes in copper levels (e.g. Erskine and Bartlett, 1993; Sangwan et al., 1993; Stabel et al., 1993; Stevenson et al., 1991) and can produce copper deficiency, a result of the increased requirements for copper in biologically important organics such as Cu-,Zn-superoxide dismutase. (Over the years, this enzyme has routinely been very heavily studied because of its role in a range of counteracting metabolic and physiological problems (e.g. Lehr et al., 1993).) Because of the importance of an adequate level of bioavailable copper, a good deal of work continues to be done on copper levels and bioavailability (e.g. Aoyagi et al., 1993a; Danon and Jakovljevic, 1992; Omoregie, 1991; Ramos Santana and McDowell, 1993) as well as the nature and effects of trace metal supplementation (e.g. Glade, 1992; Jacques and Newman, 1992; Mirando et al., 1993; Ritchie et al., 1991).

Recent literature includes a number of papers on the importance of copper in microorganisms, invertebrate animals and fish. Most of these are given elsewhere in this review. They encompass a wide range of topics including --

- the effect of copper on growth (e.g. King et al., 1992a; Prasad & Ram, 1992; Tatara et al., 1993),
- the chemical (Odermatt et al., 1993) and genetic (Thiele et al., 1992) factors affecting copper homeostasis,
- variability in tissue metal concentrations and effect of copper due to the requirements (e.g. Davis et al., 1993) and the nature of the organism (e.g. Bazylinski et al., 1993; Ishikawa et al., 1993a; Weeks et al., 1992),
- the effect of natural and anthropogenic factors (e.g. Gully & Mason, 1993) on copper concentrations,
- the nature of copper-containing compounds in organisms (e.g. Boteva et al., 1993; Opoku-Gyamfua et al., 1992), including metallothionein and the blood pigment hemocyanin (e.g. Hopkin, 1993).

A good deal of the current information about the importance of copper to humans comes from studies of laboratory animals and cell cultures. Amemiya et al. (1990) report that copper deficiency caused demyelination and dysmyelination of the optic nerve in rats, probably a result of reduced activity of copper-dependent enzymes (see Dake and Amemiya, 1991) Beneficial effects of a copper-containing organic $[Cu(II)_2(3,5\text{-DIPS})_4]$ are, for example, reported to increase survival in gamma-irradiated mice (Sorenson et al., 1993). Copper deficiency is associated with a number of physical and physiological problems in laboratory animals (many of these also in humans). These include:

Energy metabolism and body composition (Hoogeveen et al., 1993).

Physiological dysfunction (Sarricolea et al., 1993a,b; Stewart et al., 1993).

Resistance to toxic compounds (DiSilvestro & Medeiros, 1992).

Changes in activity (usually a reduction) of copper-containing enzymes (Johnson & Dufault, 1993a; Kim & Allen, 1993; Kosonen et al., 1993; Lai et al., 1993; Matz et al., 1993; Olin et al., 1993; Prohaska et al., 1993; Sergeant & Johnson, 1993).

Cell morphology and ultrastructure (Akers & Saari, 1993; Harland et al., 1991; Percival et al., 1993b; Rao et al., 1993a,b; Richmond & Chi, 1993; Scott et al., 1993; Villa Elizaga et al., 1992; Weaver, 1991 - Ph.D. thesis).

Cell metabolism (e.g. Bode et al., 1993; Farms et al., 1993; Harland et al., 1991; Lin et al., 1993a; Morin et al., 1993; Reaves et al., 1993; Scott et al., 1993; Van den Berg et al., 1991).

The chemistry of cell products (e.g. Andon et al., 1992; Luhrsen et al., 1993; Lynch & Klevay, 1993; McCoy et al., 1993).

Antibody production (Nakagawa et al., 1993b).

Calcium transport and mobilization (Johnson & Dufault, 1993a; Yamaguchi, 1993).

Variability in response to marginal or low levels of dietary copper can occur in laboratory animals (e.g. Klevay and Saari, 1993) which must be considered in evaluating the biological effect of the metal. Part of this appears to be a result of dietary factors other than the amount of copper (e.g. Schelkoph et al., 1993). Lure et al. (1993) and Fields et al. (1993a) report that the amount of dietary protein as well as the type of carbohydrate can play a role in the expression of copper deficiency. Combine this with metal-metal interactions that can occur during experiments (e.g. Werman and Bhathena, 1992) as well as dietary lipid levels (e.g. Wapnir and Devas, 1992, 1993) and the complexity of the situation becomes more apparent. There can be an effect of exercise (DiSilvestro et al., 1992) and physiological stress (Bui et al., 1993; McDermott et al., 1993), an interaction with drugs (e.g. Kishore et al., 1993) and even a potential gender effect (Werman and Bhathena, 1993a) and time of diet introduction (Lewis et al., 1992a) in rats in the copper-carbohydrate interaction.

A great deal of work has been done on the role of copper in the cardiovascular system, with laboratory animals serving as models of the human cardiovascular system. Medeiros et al. (1993a) reviews copper deficiency and cardiomyopathy, commenting (introduction) that "Copper is an essential element known to exert an influence upon cardiac pathology and metabolism". One of its roles is acting as an antioxidant nutrient for cardiovascular health (Allen and Klevay, 1994). Once again, interacting factors such as exercise (e.g. Davidson et al., 1993a,b) or the type of dietary carbohydrate and metal-metal interactions (e.g. Fields et al., 1993b) can complicate an understanding of the roles of copper. Several papers discuss the effect of copper deficiency on cholesterol and other chemicals associated with cardiovascular problems (e.g. Al-Othman et al., 1993; Koo and Yang, 1993; Koo et al., 1993; Lei et al., 1993; Medeiros et al., 1992; Nassir et al., 1993). Other references address the effect of copper deficiency on the heart (e.g. Chao et al., 1993; Chao and Medeiros, 1993; Matz et al., 1993; Medeiros et al., 1993b,c; Meissner, 1991; Williams, 1992a) or on the functioning of major blood vessels (e.g. Blake et al., 1993; Megaw et al., 1993).

The uptake, transport and metabolism of dietary copper in laboratory animals continues to sponsor a good deal of work other than on the effects of dietary components. Distribution is usually based on either the localized requirements of the metal (e.g. Sakai et al., 1993b) or its storage until used or excreted. The role of organics such as ceruloplasmin, in transporting copper can be affected by the physiological state of the organism (e.g. Nakagawa et al., 1993a,b; Yamada et al., 1993a).

The effects of copper deficiency in humans are discussed in Chesters and Arthur (1988) review of "Early biochemical defects caused by dietary trace element deficiencies." The potential for copper depletion has been suggested to be increased in rapidly growing infants (Burns et al., 1993), a time when adequate copper is important (e.g. Specker et al., 1992) and may require dietary supplementation in a suitable form (e.g. Hurley and Lönnerdal, 1988). In an interesting discussion of the use of a vegetarian diet to control Wilson's disease, Brewer et al. (1993a) comment that as a result of the marginal copper intake in American diets, a mild copper deficiency may occur with vegetarians. (This is related to the reduced bioavailability of copper in vegetarian as opposed to meat sources.) Deficiencies also occur as a result of physiological stress as, for example, during parenteral nutrition (e.g. Frankel, 1993; Matsuda et al., 1990, 1992; Okada, 1991). Dietary copper deficiency has been associated with irregular nutrient metabolism (e.g. MacDonald et al., 1991) and a number of diseases (e.g. Saari and Bode, 1993). Low levels of zinc and copper intake and high levels of calcium intake have been implicated as possible risk factors for esophageal cancer among vegetarians (Chen et al., 1992b). "Establishing reliable nutrient requirements for individuals over the age of 65 years is a difficult task" (abstract, Kerstetter et al., 1993). Health care for the elderly includes adequate dietary copper and other trace metals, a condition that is often missing (e.g. Goren et al., 1993) although Ausman and Russell (1991) comment that copper requirements may be below the usual intake of 2-3 mg/d. One factor that is often not considered, however, is that dietary copper intake requirements may differ between men and women (Johnson et al., 1992). They may also differ between individuals, as a result of the composition of the diet (e.g. Barbera et al., 1993; Randhawa and Kawatra, 1993), physical activity (e.g. Anderson, 1992a; Umoren, 1989) and genetic make-up (Milne et al., 1991). The differences can be expressed in several ways as, for example, in the abundance of the copper transport organic ceruloplasmin (e.g. Harris, 1993). Physiological state also enters into this problem because ceruloplasmin activity normally increases during infections, inflammatory diseases, and neoplastic diseases (Manjula et al., 1992; Miesel and Zuber, 1993b; Natesha et al., 1992; see also Aselderova, 1992). (However, a decrease has been reported in Alzheimer's disease patients (Connor et al, 1993).) Changes can occur in other copper-containing organics (e.g. Cu-,Zn-Superoxide Dismutase) as a direct or indirect result of disease (e.g. Kikkawa et al., 1992; Miesel and Zuber, 1993a) or treatment of the disease (e.g. Küpeli et al., 1993).

Copper is involved in connective tissue formation and maintenance. Deficiency of the metal can be associated with abnormal skeletal development in young children (e.g. Nii et al., 1991; Paterson et al., 1993) and postmenopausal bone loss in women (Howard et al., 1992; Saltman, 1992; Saltman and Strause, 1993; Strause and Saltman, 1993). With infants, copper supplementation is often advised to reduce the chances of bone mineral disorders like rickets (Takada et al., 1992) or periosteal hyperostosis (Yasufuku et al., 1991). There is increasing evidence of involvement of trace metals such as copper, in movement disorders such as Parkinson's disease (e.g. Zecca and Swartz, 1993).

The nature of copper-containing inorganic (e.g. Sorenson, 1992b) and organic complexes forms the basis for a large number of recent references, a result of the biological importance of these complexes. A good deal of this literature involves complexes that provide tools to examine chemical processes (e.g. Ozawa et al., 1992) or are metabolically important (e.g. Chen et al., 1992d; Gross, 1993; Kelly et al., 1993; Paul-Eugène et al., 1992) (or are valuable from both standpoints). Many of the metabolically important references deal with the activity and structure of enzymes (e.g. Ensign et al., 1993; Keshavarzian et al., 1992; Kitajima et al., 1993b; Lappalainen et al., 1993; Pitari et al., 1993; Saiki et al., 1993; Shah et al., 1993; Wang et al., 1993b; Woodruff, 1993). Copper is involved with strong oxidizing systems in the body (e.g. Casella et al., 1992). Of particular interest is Cu-,Zn-superoxide dismutase (SOD) which protects cells against superoxide radicals resulting from oxidoreductive cell metabolism (Favero et al., 1992; Ishikawa et al., 1993b; Steinman, 1993; Voegeli et al., 1993). The role played by copper in lipoprotein metabolism is becoming of increasing importance in understanding cardiovascular problems such as atherosclerosis (e.g. Sakai et al., 1992; Tanaka and Kanamaru, 1993). Other copper-organic interactions which have recently been studied include the interaction between dietary copper and carbohydrates (e.g. Bhathena et al., 1991) and the interaction of pharmaceutical agents and organometallic complexes (e.g. Kirkova et al., 1992a,b).

I.3 BIOLOGICALLY IMPORTANT USES OF COPPER BY HUMANS (* = patent document)

The requirement for copper has sponsored a good deal of work on appropriate metal concentrations and bioavailability. Copper is often added to fertilizers to serve as a supplement to plants. It is also used in seed dressings either as a nutrient supplement or to reduce the potential for disease. The following references and patent applications are examples of recent literature that discuss the use and benefits of the metal:

<u>Fertilizers</u> - Akl et al., 1993a,b; Benemann, 1992 (review of "The use of iron and other trace element fertilizers in mitigating global warming"); Brockley, 1992; Evans et al., 1992a; Kovaleva et al., 1994; Kovalevich et al., 1991; Nedilko et al., 1992*; Ojeniyi & Kayode, 1993; Onyezili & Harris, 1993; Peng et al., 1992*; Przepiorka et al., 1991*; Sadiq & Hussain, 1993; Sharma et al., 1992; Sheudzhen et al., 1991a; Stiles & Rutzke, 1993; Tadano et al., 1992; Takahashi et al., 1991; Trehan & Grewal, 1994; Tyksinski, 1987a,b; Varadachari, 1992; Willems et al., 1993b; Zhang, 1993*; Zhang et al., 1992f; Zhu & Li, 1991.

<u>Preplanting treatment</u> - Dzhemilev et al., 1992*; Maeda, 1993*

<u>Fertilizer types/production and delivery/application methods</u> - Dankiewicz et al., 1992*; Feng, 1992*; Guo, 1992*; Konishi et al., 1993*; Li & Gao, 1992*; Ming & Galden, 1993*; Morvedt

& Mikkelsen, 1993*; Nowosielski et al., 1992*; Trojan & Brandova, 1992*; Wolski & Gawecki, 1992*; Xing, 1992*; Ye et al., 1993a*;Ye et al., 1993b*; Yokoyama & Koyanagi, 1992*; Zekri & Koo, 1992

Copper is an obvious requirement for domestic animals (e.g. Grace & Lee, 1988; Lee & Grace; Ramos Santana and McDowell) and deficiency is a potential problem that must be considered. The following references are examples of recent literature that discusses the nature and effects of supplementation:

Feed supplements - Ali & Al-Noaim, 1992; Ashmead et al., 1992*; Blincoe, 1993b ("Computer simulation of copper pharmaceuticals in cattle"); Bowland, 1990; Dolgov, 1992*; Dove, 1993a; Fazekas et al., 1993*; Fujimoto et al., 1993 (effect of copper on prostaglandin synthesis); Gaffarov et al., 1990; Gorobets, 1991; Imanov et al., 1992*; Kim & Paik, 1993; Kim et al., 1991, 1993; Li & Wu, 1992; Liu et al., 1992*; Matsui et al., 1992; Paik et al., 1991; Spiekers et al., 1991; Treuthardt, 1992; Ward et al., 1993a; Yen & Nienaber, 1993; Yen & Pond, 1993; Zelenak et al., 1992; Zholbolsynova et al., 1992*.

Bioavailability of copper in supplements - Aoyagi & Baker, 1993a,b,c

Supplements for arthropods (e.g. bees) - Guerrero et al., 1993; Vashakidze et al., 1993*

Adequate dietary copper is essential for normal physiological condition in humans. Recent references on the requirements for copper include work on laboratory animals and humans:

Laboratory animals - Ashmead, 1993*; Werman & Bhathena, 1993a,b

Humans - Bogden et al., 1993; Uehara et al., 1991; Yatsula et al., 1992*

Copper continues to be an important component of a numer of pharmaceutical agents, as a radionuclide for imaging purposes, in copper laser treatment of certain types of abnormal growths in humans, medical instruments/equipment and techniques. Pharmaceuticals include across-the-counter drugs as well as prescription drugs.

Pharmaceutical agents and their analysis - Arimoto et al., 1993; Badawy et al., 1993; Barni et al., 1992; Cao et al., 1992; Chohan & Siddiqui, 1993; Connett et al., 1992; Crispens & Sorenson, 1992b; Douglas et al., 1991; Durán et al., 1993; El-Saadani et al., 1993; Emerit et al., 1991; Fairlie & Whitehouse, 1991; Felix et al., 1993; Franco et al., 1992; Goel et al., 1992 (discussion of traditional Indian preparation of copper for ulcer treatment); Green et al., 1991; Kozlowski et al., 1992; Kuncheria & Aravindakshan, 1993; Miesel, 1992b; Mohan & Nagar, 1992; Nakamura & Yasuda, 1992*; Pal et al., 1993a,b; Selman et al., 1993; Shlyakhovenko et al., 1991; Shoukry, 1992; Sokolík et al., 1992a,b; Sordelli et al., 1993; van Rooijen & Poppema, 1992; Wahlund et al., 1992; West et al., 1993b; Wu et al., 1991b (pharmacokinetic study of oral copper gluconate and copper sulfate); Ye et al., 1993c; Zhang et al., 1991a.

Control of enteric pathogens in water - Bosch et al., 1993; Colville et al., 1993 (Outbreak of Legionnaires' disease in a hospital - controlled by installation of an electrolytic agent releasing silver and copper ions into domestic hot water in the wards).

Agents for use in veterinary medicine - Melnik, 1991*

Drugs to protect against radiation - Jagetia et al., 1993; Sorenson, 1992a (a good review of metalloelement metabolism and radiation protection and recovery).

Copper as one of several trace elements useful in burn treatment - Berger et al., 1992a

Other agents in medicine and the production of medications - Kurchacova & Yip, 1993; Wu, 1992b

Radionuclide use - Anderson et al., 1993a,b,c,d,e; Borman et al., 1992; Connett et al., 1993; DeNardo et al., 1993; Fujibayashi et al., 1993a; Goins et al., 1993; Green, 1992; Green et al., 1991, 1993; Herrero et al., 1993; Mathias et al., 1993; Mirzadeh et al., 1993; Philpott et al., 1993; Shen et al., 1993b; Wahl et al., 1993; Yim & Meyerhoff, 1992

Medical instruments/equipment and techniques - de F. Santos & Weinreich, 1993; Kupka et al., 1992; Li, 1992b; Li & Trush, 1993b; Yokono et al., 1992; Young et al., 1993

Copper vapor laser uses - Lantz et al., 1992; Lapins et al., 1993; Nemeth et al., 1993; Neumann et al., 1993; Sheehan-Dare & Cotterill, 1993; Sinev et al., 1991.

Dental uses of copper include amalgams, mouthwashes and toothpaste. References discussing this array of agents include:

Drake et al., 1993; Johnson & Powell, 1992; Marek, 1992; Marshall & Marshall, 1992; Osborne et al., 1993; Taylor et al., 1993a; Torstenson & Brännström, 1992; Veronesi et al., 1992.

Copper continues to be used as an effective contraceptive agent although the nature of its effect is not well understood. Almost all of the recent literature considers intrauterine devices (IUD), many of which use copper as the principal agent:

Amla et al., 1993; Bergsjø, 1992; Bozzini et al., 1991; Brosens et al., 1991; Chi, 1992; Díaz et al., 1992a,b; ; Díaz et al., 1993; Edelman & Porter, 1993; Fraser, 1992; Kimmerle et al., 1993; Kjaer et al., 1993; Luukkainen, 1992; Parazzini et al., 1992; Parra et al., 1991; Sivin, 1993; Sivin et al., 1991b, 1993; Tiwari & Angra, 1991; Tsong & Nash, 1991; Van Dierendonck et al., 1992; Wagatsuma et al., 1992; Wang et al., 1992a.

The growth of organisms on structures in the water and in the ground can drastically increase the rate of decay of the structures. In aquatic situations, fouling reduces water flow and is responsible for increased fuel costs in vessels and pumping systems as well as reduced water exchange in cooling systems. Copper is an effective antifoulant and continues to be widely used:

Wood preservatives containing copper for terrestrial environments - Feist & Ross, 1988; Gjovik & Schumann, 1991; Goettsche & Borck, 1992*; Hager, 1993*; Johnson & Thornton, 1991; Kumar & Dobriyal, 1992; McLaughlan, 1991; Nagano, 1993a*,b*; Vick & Kuster, 1992.

Antifouling compounds in aquatic environments - Hasegawa & Kurashige, 1992*; Ikari & Takahashi, 1993*; Kakehashi, 1992*; Karande et al., 1993; Kumar et al., 1991; Rao et al., 1993c; Yoshida et al., 1993b.

Other "antifouling" types of uses - Hayama et al., 1993* (metalion-intercalated layered phosphate compounds as antimicrobial agents for industrial use); Honda & Kaetsu, 1993* (copper in acrylic polymers for bactericidal and fungicidal use); Kani et al., 1993* (bactericidal and fungicidal agents); Maki, 1992* (microbicide sheets for domestic use); Martin et al., 1992 (lichens on asbestos cement roofing); Murasawa et al., 1993* (antimicrobial and rust-controlling materials for refrigerators); Piterans et al., 1992 (vegetation on monuments); Thomas, 1993* (algae-resistant edge coating for cooling towers and evaporative coolers); Tomioka et al., 1993* (antibacterial and rust-preventing coatings for stainless steel products); Yagi et al., 1993 (antimicrobial and rust-controlling materials for bathrooms).

In aquatic situations like farm ponds, aquatic weed plants can be detrimental. Excessive growth will reduce water exchange and increase the amount of organic matter and the biological oxygen demand of the system. References on the uses of copper to control weed growth include:

Augier et al., 1992b; Dyer et al., 1992; Haglund & Pedersén, 1993; Hirono et al., 1991; Lan et al., 1992; Swain & Adhikary, 1991 (control of blue-green algal species in laboratory cultures).

The ability of copper to control growth has been used by nurseries to control root growth. Recent references include:

Beeson & Newton, 1992; Flanagan & witte, 1992; Krieg & Witte, 1993; Latimer, 1993; Svenson & Broschat, 1993;

Copper is widely used to control the growth of noxious or detrimental organisms (bactertia, fungi, plants, animals) in terrestrial environments. Recent references include:

<u>Bactericides and fungicides</u> - Anandaraj & Sarma, 1991; Atsumi et al., 1992*; Beresford, 1992; Bláhová et al., 1991, 1992; Blum & Gabardo, 1993; Böhland et al., 1990; Chakrabarty, 1993; Chen, 1992a*; De Cal & Melgarejo, 1992; Dethe et al., 1993; Dimova-Aziz, 1990; Dubearnes et al., 1992*; Florianowicz, 1991; Gaignard et al., 1993; Gerritse et al., 1992; Gomez, 1991; Hartill, 1992; Ipach, 1992; Kassim, 1992; Kato, 1992; Kokosková, 1992; Koomen et al., 1993; Kuczynska, 1989; Laker & Ram, 1992; Lee et al., 1992; Lonsdale & Kotzé, 1993; Lopes de Castro et al., 1991; Maheshwari et al., 1991; Martinez-Ferrer et al., 1991; Mathur & Sobti, 1993; McGrath et al., 1993b; Mosch et al., 1990; Moustafa-Mahmoud & Sumner, 1993; Nakanaga et al., 1992*; Nakashima et al., 1991, 1992; Nene & Thapliyal, 1993 (book on "Fungicides in Plant Disease Control"); Nogueira, 1991; Obata et al., 1992; O'Brien, 1992; Olson et al., 1992; Olufolaji, 1993; Parman et al., 1991; Patel & Patel, 1991, 1992; Patel et al., 1991; Redl, 1993; Revellin et al., 1993; Sakauramoto, 1993*; Schroth et al., 1993*; Senda & Tateishi, 1992a*,b*; Sharma, 1992; Sheen & Langley, 1993*; Sheudzhen, 1991c; Shibata & Hiramatsu, 1992*; Slade & Pegg, 1993; Smith & Papacek, 1991 (A study of the effect of pesticides on a useful predatory mite in citrus orchards. Copper oxychloride was one of the two pesticides that did not adversely affect the abundance of the mite which is a predator on a citrus rust pest.); Sobiczewski & Berczynski, 1990; Sokolík et al., 1992c; Solarska & Pietrzak, 1989; Soyez, 1992a,b; Sugha & Singh, 1992; Sugha et al., 1993; Sun et al., 1991; Sundin & Bender, 1993; Szava, 1993*; Takatori & Hattori, 1992*; Taylor & Crawford, 1993*; Toth et al., 1992*; Trocmé, 1991; Utkhede & Smith, 1993; Varshney et al., 1991; Wada et al., 1992*; Wang, 1992; Yamagishi & Tsuchizawa, 1993*; Yamamoto et al., 1991; Zemtsova et al., 1992*.

<u>Molluscicides</u> - About-El-Hassan et al., 1990; Al-Sabri et al., 1993; Kumar et al., 1992; Rondelaud & Vareille-Morel, 1994; Secor et al., 1993 (bioaccumulation of toxicants in zebra mussels).

Miscellaneous - Parshad et al., 1993 (use of copper oxychloride fungicide as a rat repellent); Straus, 1993 (use of copper sulfate to control of ectoparasite infestation in catfish fingerlings); Tagawa, 1993a*,b* (fish parasite control)

Because of its malleable nature, copper has long been used for human artifacts as well as instruments. Discussions of early copper metallurgy have benefited from improved analytical techniques which not only better allow examination of the evolution of copper metallurgy (e.g. Fleming and Swann, 1993) but also the ability to identify the source of copper artifacts (e.g. Hancock et al., 1993). Today's use of copper is at record levels as indicated by the record 1991 consumption of 10.8 million tons (Jolly, 1993) even with the effects on metal values of economic slowdown (e.g. Peterson and Cappa, 1993).

With regard to metal extraction, Lankton (1991) provides an interesting and well-written discussion and history of the copper mining "communities" in the Keweenaw Peninsula of upper Michigan. Physical properties of the metal also make it an excellent conductor and tubing material. Recent references on the latter are limited because of the nature of the review. Several did appear, as well as discussions of ancient mining and smelting sites/techniques:

Ancient copper production - Craddock, 1992; Fleming & Swann, 1993; Hancock et al., 1993; Piaskowski, 1991.

Tools, materials, tubing and conductors - Capelato, 1993; Jorgensen et al., 1993; Koster, 1993; Lyle, 1993; Rapp, 1993; Shams El Din, 1993a,b; Yokono et al., 1992.

Miscellaneous - Lee & Kang, 1989; Santee et al., 1993.

The ability of copper to combine with organics has made it widely used in chemistry, to examine some of the fundamental chemical concepts, to determine the nature of organometallic compounds (and the organisms that produce them), to synthesize potentially useful agents and to assist in purification of noxious chemicals/fuels. Because of its reactive nature, copper is also used in a wide range of chemical purifications and rections. Some examples of recent work are given here, the majority are found in a later section on biologically important copper-containing organics:

Copper in organics - Barbas et al., 1993; Craik et al., 1992; Grabbe & Cordes, 1993; Jungblut et al., 1993; Kawai, 1993a,b;

et al., 1993; Mercado-Blanco et al., 1993; Monti et al., 1993; Phelps et al., 1992; Ryan et al., 1993; Watabiki, 1993; Woker et al., 1992; Yde, 1993.

Uses in chemical work and as preservatives and stains in biological work - Achar et al., 1992; Arnold et al., 1992; Baumgartner, 1993; deMontigny et al., 1993; Ersoz et al., 1993; Floyd et al., 1993; Furbee et al., 1993; Gysemans & Mertens, 1993; Jiang, 1992*; Jiménez-Prieto et al., 1992; John & Douglas, 1993; Lahuerta Zamora & Calatayud, 1993; Lesser & Guthrie, 1993; Luo & Baldwin, 1992; Luo et al., 1993a; Matsushita et al., 1993; Polycarpou-Schwarz & Papavassiliou, 1993; Pugia & Salvati, 1992*; Root, 1992 (Ph.D. thesis); Saito, 1992; Sayato et al., 1993; Seijas et al., 1992; Tsuji et al., 1993*; Van Heusden, 1993; Wang & Root, 1993.

Uses in preparation/preservation of food and drink materials (discussed under food and food chains) including colour preservation in natural products - Cotterill et al., 1992; Lee & Chang, 1991; Pilková et al., 1990; Redl, 1992; Refsgaard et al., 1992; Singh et al., 1992c; Vervaeck et al., 1992*

Purification of noxious agents - Abmann, 1992; Browne & Robertson, 1993*; Chang et al., 1993a; Hill et al., 1993;

Industrial uses of copper are numerous and, for the most part, outside the scope of this review. However, the scope does include the use of copper in classroom demonstrations, the application of copper as a reactant (e.g. nitric oxide decomposition) and the use of the metal in container materials for long-term storage of nuclear waste mateirals. Recent references include:

Classroom demonstrations - Matsuyama et al., 1991; Ricketts & Schwartz, 1992.

Copper as a reactant -Flytzani-Stephanopoulos et al., 1993; Raikar et al., 1993.

Other Industrial uses - Olesik, 1990, 1992; Sakurai et al., 1993b*

I.4 COPPER CONCENTRATIONS IN ORGANISMS

I.4.1 Physiologically Normal Organisms

The concentration of copper in the tissues of an organism is controlled by the physiological condition of the organism and the chemical state of the copper. The ability of an organism to regulate the uptake and metabolism of copper as well as the excretion or storage of excess metal is affected by physiological well-being. Physiologically normal organisms represent natural conditions, abnormal organisms provide an indication of the effects of stress on tissue metal concentrations. The chemical state of the copper dictates metal bioavailability, a condition which must be considered -- independently from the concentration of metal in the environment. Some of these concepts are examined in review publications which have recently appeared (Adriano, 1992; Linder, 1991), publications which examine metal geochemistry (e.g. Miramand, 1993). They are also considered in the numerous publications on metal uptake by organisms (see National Technical Information Service, 1993a,b). They need to be considered in any surveillance project, including those covering large geographic areas (e.g. Sen Gupta et al., 1989; Varanasi et al., 1989)

Variability in uptake, organism metal levels and metal tolerance is found in microorganisms, plants and animals. As an example, with mushrooms, Borella et al. (1991) comment (English summary) "... that mushrooms are able to selectively concentrate different metals, and that both the mushroom characteristics and the geographical area of collection could play a role in the mechanism of accumulation." Although details of copper uptake, such as rate of uptake and transport, tend to be group or even species specific (e.g. Cowgill and Landenberger, 1992; Novacek, 1987b; Pan, 1991; Wojcieska et al., 1989) as well as affected by growth stage (e.g. Novacek, 1988; Ogunmoyela and Esan, 1990, general comments can be made about the nature of uptake and metabolism (see section on metal uptake). Tolerant microorganisms and plants that are effective accumulators of copper have been proposed or used as a means of recovering copper from tailings as well as industrial effluents (e.g. de Silóniz et al., 1993; Wong and So, 1993). (Boyd and Martens (1992) present an excellent discussion of hyperaccumulation by plants.) Soil metal content and bioavailability can vary as a result of a variety of climatic, geochemical and biological factors as well as the nature of the metal (e.g. Barros Henriques and Hay, 1992; Hocking, 1993a; Hogg et al., 1993; Jugsujinda and Patrick, 1993; Kim and Thornton, 1993; Pertoldi-Marletta et al., 1991; Ruszkowska et al., 1990, 1991; Tagliavini et al., 1993; Vazquez de Aldana et al., 1993; see also Jackson and Kalff, 1993 for aquatic plants). Expression of these factors can be seen under managed agricultural conditions (e.g. du Preez and Bennie, 1992a; King et al., 1992b) as well as in natural conditions.

The interaction of microorganisms and metal-containing environments such as bogs (or amended soil) has been reported to affect metal chemistry (Farago and Mehra, 1993; see also Singh et al., 1991) and would have an effect on bioavailability. The effect of microorganisms on plants includes tissue metal concentration as well as the biochemistry of both microorganisms and plants (e.g. Lee et al., 1991d; Régius-Mosényi and Anke, 1992). However, some plants exhibit the ability to adapt to conditions of nutrient deficiency (e.g. Bowen and Macomber, 1993) or excess. Tolerance of high levels of biologically available metal is not uncommon in plants found in areas of mineralization (Punz, 1992), some of which can be used as indicators of metal deposits.

The use of wastewater or residue from sewage, for plants, can provide increased concentrations of metals to soils although metal bioavailability will be affected by the metal-organic associations in the soils (e.g. Narwal et al., 1992; Pérez and Gallardo-Lara, 1993). The use of organic and inorganic fertilizers will produce quite different tissue metal concentrations (e.g. Browaldh, 1992) that is dependent on the chemistry of the fertilizers, the nature of the soil and the nature of the plant (e.g. Nus et al., 1993; Spiers, 1993). Fortunately, this has stimulated the development of specialized nutrient materials to match the nature of the plant (Menzel et al., 1993). Coal bottom ash, when used in a plant growth medium, is reported to be associated with copper deficiency (Bearce, 1993). Aerosol input of metal, to soils or directly to plant surfaces, can also occur (e.g. Zayed et al., 1992). However, plant uptake of anthropogenic copper from soils is dependent on the same factors as uptake of naturally-occurring copper. A change in soil pH can, for example, produce a major change that affects metal mobility, bioavailability and the potential for uptake (e.g. Rinallo et al., 1993). Differences in uptake have not only been reported as a result of differences between species of plants (e.g. Lukaszewski et al., 1993) but also differences between populations within a species of plant (Ogner, 1993; Rachwal et al., 1992). In aquatic as well as terrestrial plants and animals, changes that occur during the life history will affect tissue metal concentrations (e.g. Fasidi and Kadiri, 1993; Ryczkowski and Reczynski, 1991; Slipcevic et al., 1993) as will seasonal changes in the organism as well as the bioavailability of the metal (Gallardo et al., 1991; Hocking, 1993b; Rao, 1992a; Yang et al., 1992). An additional complicating factor is that seasonal changes in the composition of the biological community can also affect environmental metal concentrations and bioavailability (e.g. Sfriso et al., 1992), a sort of feedback loop that needs to be considered when examining the potential impact of anthropogenic copper. The mineral content of plants grown under elevated CO_2 conditions are reportedly lower, a factor that would provide long-term effect due to changing atmospheric conditions (Peñuelas and Matamala, 1993).

Tissue copper concentrations have been measured in a range of invertebrate animals (see tabular data in this review) and have been proposed or used as indicators of environmental conditions, including metal bioavailability (e.g. Baudo and Galanti, 1988; Cain et al., 1992; Naimo et al., 1992). Differences are routinely found between species of invertebrates (e.g. Ikuta, 1991b; Mariño et al., 1992); those which use hemocyanin, for example, will often have above average concentrations of copper (Roth, 1992). Within a species, differences in tissue copper concentrations have been reported depending on where it is found and when it is collected (i.e., spatially and seasonally) (e.g. Bordin et al., 1992; Canli and Furness, 1993a; Joseph and Srivastava, 1993; Marmolejo-Rivas and Páez-Osuna, 1990; McEvoy and Sundberg, 1993; Mitra and Choudhury, 1992b, 1993b) as well as physiological condition (e.g. Ireland, 1993; Scottt-Fordsmand and Depledge, 1993; Vernon et al., 1993; Weeks et al., 1992), the state of its development or growth (e.g. Chowdhury and Singh, 1993; Gintenreiter et al., 1993a; Vernon et al., 1993; Weeks et al., 1992) and sex. Although tissue levels of copper and copper-containing organics are often higher in individuals collected from sites of elevated metal levels (e.g. Engel et al., 1993; Ikuta, 1991c), the concentration of metal does not necessarily relate directly to the concentration in the environment. This is a result of metal bioavailability or metal-metal interactions (the environment) (e.g. Batley et al., 1992; Nell and Chvoka, 1992; Perdicaro, 1989), variability in tissue metal concentration (Nolan, 1991) and an ability to regulate metal uptake (the organism) (e.g. Morgan and Morgan, 1992) as well as metabolism. The ability to regulate tissue metal levels may not be universal (e.g. Verdenal et al., 1990) but it is indicated by the differences in metal concentrations between sites (e.g. Fuge et al., 1993) and organs within an individual -- copper concentrations are typically elevated where storage and/or excretion occurs (e.g. Canli and Furness, 1993a,b; Dious and Kasinathan, 1992; Martoja and Marcaillou, 1993). Viarengo and Nott (1993) provide an excellent review of metal regulation in their publication "Mechanisms of heavy metal cation homeostasis in marine invertebrates". As would be expected, there is evidence that genetic factors are responsible for the extent to which copper is accumulated (e.g. Alikhan, 1993).

In vertebrates, other than domestic animals, laboratory animals and humans, factors affecting tissue copper concentrations are similar to those in invertebrates and, to a considerable extent, plants and microorganisms. As expected, there are differences between species (Frank et al., 1992a) and between individuals from different locations (e.g. Hecht, 1992) or collected at different times of the year (e.g. Metayer et al., 1992). Metal-metal interactions may also affect copper uptake and tissue metal concentrations (e.g. Kargin et al., 1992). Differences in concentrations have been reported as a function of body weight (e.g. Rottiers, 1993) and length (Evans et al., 1993). In the barn owl, Denneman and Douben (1993) note an increase in copper concentration with age in the primary wing feather used for the study. Changes with age (e.g. Hillis and Parker, 1993; Wlostowski, 1992) and sex (e.g. Pankakoski et al., 1993) have also been noted in other types of vertebrates although the changes with age may be either increases or decreases. Higher tissue levels have been reported in individual specimens from areas of elevated levels of metal (e.g. Khan and Weis, 1993) and specimens exposed to environmental stress (Halbrook et al., 1993). Evidence of metabolic control over tissue metal levels continues to be presented in fish (e.g. Kowalewska and Korzeniewski, 1991; Malyarevskaya and Karasina, 1991), birds (Lewis et al., 1992b) and mammals although Hyvärinen and Nygren (1993) provide evidence of poor regulating ability in moose. Emara et al. (1993) report a tendency for higher levels of essential metals (Mn, Fe, Cu) in fish at higher trophic levels although they suggest that metabolic control does occur.

Tissue copper concentrations in domestic animals can vary between species (e.g. Anderson, 1992b) and within a species, in contrasting habitats (Wallis de Vries, 1992) or as a result of seasonal changes (e.g. Wildeus et al., 1992). Within species variability can occur as a result of genetic characteristics of the breed (Littledike and Young, 1992, 1993; Littledike et al., 1993) as well as conditions associated with the environment or the management practices used (e.g. Elbers et al., 1992). Tissue copper concentrations can also change within an organism as a result of food quality or physiological status (e.g. Abdelrahman and Kincaid, 1992; Migdal et al., 1993), or metal-metal interactions (e.g. Kolb et al., 1992a). Physiological changes can occur during development (e.g.Proske et al., 1993; Richards, 1991b), as a result of events during the reproductive cycle in the adult, seasonal changes in habits and habitat or as an effect of medication (e.g. Lü and Combs, 1992). These are all important and have sponsored a good deal of work on requirements and nutrient quality (e.g. Bozic and Gvozdic, 1993; Edmiston and Bull, 1993; Hemingway, 1991; Kume and Tanabe, 1993; Lee et al., 1991a; Xin et al., 1993a). This includes continued work on the balance between copper, molybdenum, selenium, zinc (et al.) necessary in sheep and cattle in areas with elevated or deficient levels of the metals (e.g. Angelow and Yanchev, 1991).

Laboratory animals are used as convenient models of human physiology or as mechanisms to measure the impact of some factor on a mammal maintained under laboratory conditions. They have been used to examine the distribution of copper or copper-containing organics in cells, tissues and organs (Coursin et al., 1992; Falnoga et al., 1991; Kodama, 1992; Larsen and Sandström, 1992b; Liou et al., 1993; Uehara et al., 1991). Laboratory animals are used to examine the effects of food materials on tissue metal distribution (e.g. Gunshin et al., 1990; Kashimura et al., 1992; Kohls and Douglas, 1993; Shah, 1991; Uehara et al., 1987, 1988). Changes in tissue copper concentrations have been related to physiological conditions occurring during the normal reproductive cycle and pregnancy (Sangha et al., 1993; Wachnik et al., 1993), during gestation (Munim et al., 1992), as a result of exercise (Lewis et al., 1993b) or abnormal conditions which affect the copper status of the organism (e.g. Wilson's disease - Kubota et al., 1991).

As an essential element, serum copper concentrations have been used in evaluations of trace element status in humans (e.g. Ando et al., 1991; Hongo et al., 1993; Milman et al., 1993; Zhu et al., 1991b). Other easily-measured materials include deciduous teeth (Shimizu, 1992), skin (Kobayashi et al., 1993) and hair (Donma et al., 1992; Moro et al., 1992; Sandford and Kissling, 1993; Sturaro et al., 1993a,b; Watanabe et al., 1992; Umebayashi et al., 1990). Sandford and Kissling (1993) note that hair samples from medieval Nubian remains indicate possible dietary as well as age-related trends and diachronic differences. A variety of other tissues have been examined, either by noninvasive techniques or post-mortem (e.g. Amemiya, 1989; Amemiya et al., 1990; Caroli et al., 1988; Fu et al., 1992; Maenhaut et al., 1993; wender et al., 1992). Problems with the use of tissues and easily-measured materials do exist and can affect the measurement and the interpretation of data for both recent and ancient samples (e.g. Elliott and Grime, 1993; Pyatt et al., 1991; Sturaro et al., 1993; Yoshino et al., 1993). As with other organisms, differences in tissue copper concentrations (or concentrations of copper-containing organics) can be a result of age, sex and physiological state of humans (Ahmed et al., 1993; Ausman and Russell, 1991; Clemente et al., 1992; Johnson et al., 1992b; Milne et al., 1991; Milne and Johnson, 1993; Musci et al., 1993b; Nagra et al., 1991; Natochin et al., 1990; Niwa et al., 1993; Wasowicz et al., 1993; Yabuki et al., 1991), including the levels of copper-containing agents in human milk (Anderson, 1993; Kiyosawa et al., 1993; Ohtake and Tamura, 1993) (see tabular data for values). Evidence continues to accumulate, on the importance of metal-metal interactions in affecting copper levels in humans (e.g. Leung and Li, 1993; Lutz et al., 1992). Substantial copper losses can occur during strenuous exercise and may require supplementation if intake is inadequate (e.g. Anderson, 1992a; Bordin et al., 1993; Nuviala Mateo et al., 1991; Ohno et al., 1993). However, this will vary depending on the age and physiological makeup of the individual (e.g. Shiraishi et al., 1992b).

I.4.2 Physiologically abnormal Organisms

Stress in microorganisms, plants and animals can affect the uptake, metabolism and tissue levels of metals, including copper. As an example, Cabral (1992) reports the production of a strong copper-complexing agent by a starved microorganism (*Pseudomonas syringae*). Stress in plants can be due to a variety of causes including saline water (Padole, 1991), elevated nitrogen in sewage sludge-ammended soils (Obbard et al., 1993) and excess biologically-available metal (e.g. Novácek and Sigutová, 1985). In animals, an effect from pollutants is often expressed in changes in tissue metal levels or organics containing metals such as enzymes or metallothionein (e.g. St. Louis et al., 1993). However, the relationship between pollutant concentration and effect is not always apparent (e.g. Livingstone et al., 1992), a result of environmental and biological factors. Detrimental environmental factors can affect tissue trace metal levels during embryonic development (e.g. Richards et al., 1992), growth (e.g. Bires et al., 1993) and aging. Under the conditions of the study, Bires et al. (1992, 1993) found that industrial emissions of copper can increase tissue copper concentrations and cause mortality in sheep, in part possibly a result of cellular injury due to non-specifically bound copper (Sansinanea et al., 1993). Work with nutrition under stress in domestic animals such as calves indicates the effect of stress on tissue copper concentrations (Nockels et al., 1993). Parasitic infections of domestic animals such as sheep have been associated with reduced serum copper levels (Erskine and Bartlett, 1993; Sangwan et al., 1993). However, the effects of nutritional and environmental factors on tissue metal concentrations in domestic animals can be misinterpreted. As an example, yellow discoloration and high liver copper levels in veal calves can be a result of a combination of conditions including viral and bacterial infections, low dietary iron, anaemia, miscellaneous toxins - as well as dietary copper levels (Groot and Gruys, 1993).

The effects of physiological abnormalities have been examined in laboratory animals since they are often used as physiological models for human illnesses. Results of recent work with laboratory rats, mice, rabbits and dogs includes reports of:

Nutrient deficiency effects on copper levels...... Brown & Strain, 1992; Zentek et al., 1991
A decrease in serum copper from stress and inbreeding ....Kosowska, 1992
An increase in serum copper from intratracheal administration
of dust ....Havránková et al., 1993a,b
Changes in muscle copper levels from immobilization........Laakso et al., 1991, 1992, 1993
Reduced skin copper levels after X-ray irradiation.......................................De et al., 1992
Hyperoxia elevated Cu,Zn-superoxide dismutase (SOD)................... Das & Fanburg, 1993
Changes in copper or the copper transfer agent ceruloplasmin
with injury.................Mainero et al., 1992; Ragimov et al., 1992; Vaxman et al., 1992
Abnormal liver metabolism from copper overload................................ Sokol et al., 1993b
Increases in liver copper - associated with
Hepatitis in LEC rats..Sugawara et al., 1991,1992a; Sumi et al., 1993; Takikawa et al., 1991
Parasite infection .... Matousek de Abel de la Cruz et al., 1993; Tsocheva & Gabrashanska, 1992
Iron deficiency .... Yamagishi et al., 1991
Effects of other metals on tissue copper levels.....................................Boscolo et al., 1992
Effects of metallothionein on copper distribution in cell extracts............ Farrell et al., 1993
Effects of drugs on copper metabolism or tissue copper levels..
Critchfield et al., 1993; Dewoskin et al., 1993; Hoppe et al., 1993; Krari & Allain, 1993; Tanaka et al., 1993a; Yamaguchi et al., 1992

Role of copper in cardiovascular diseases
Increase in serum copper with copper sulfate supplementation......Vlad et al., 1993
Changes in copper or SOD levels with ischemia...................... Ohtsuki et al., 1992; Yan et al., 1993
Effects of tumours on tissue copper levels.............. Jiang et al., 1991; Wei & Chung, 1993

Physiological abnormalities in humans are often expressed in tissue copper levels. As a result, levels are often examined or used as indicators of physiological condition or effect. Recent work, or results from recent work are varied and include:

Reduced plasma copper from severe malnutrition (kwashiorkor).......Subotzky et al., 1992

Effect of work-related exposure on levels of tissue copper or ceruloplasmin
Workers in maintenance of watermark moulds in a paper mill................................ Srivastava et al., 1992a
Welders .... Mongiat et al., 1992
Radiographers - increased scalp hair copper........................Chatterjee et al., 1993b

Changes in maternal or fetal tissue copper levels during and after pregnancy
Abnormal pregnancies..........An et al., 1990; Natochin et al., 1990; Zhao et al., 1992b
Maternal copper in gestational diabetes ....Loven et al., 1992
Reduced erythrocyte copper levels in newborns from Type I
diabetic mothers .... Speich et al., 1992
Reduced post-partum tissue copper levels in very low birth weight
(VLBW) preterm infants... Burns et al., 1993
Potential of reduced post-partum tissue copper levels in
VLBW infants with rickets..Takada et al., 1992
Reduced serum copper levels in infants on total parenteral nutritionYasufuku et al., 1991
Plasma copper levels in preschool children with growth impairments.... Chakar et al., 1993
Effect of skin diseases on serum copper levels....................................... Tasaki et al., 1993
Copper concentrations in cataractous human lenses................................Balaji et al., 1992;
Rasi et al., 1992; Srivastava et al., 1992b
Effect of general infection on tissue copper levels
Increased serum copper in children... Brown et al., 1993a
Copper losses resulting from burns...Berger et al., 1992b
Effect of drug-related diseases.................................Hosokawa & Yoshida, 1992; Hurd &
Wilder, 1992; Kuzuya et al., 1993

Effect of parasite infection
Increase in brain copper levels with bacterial meningoencaphalitis......Yarosh, 1992
Increased liver copper in *Schistosoma mansoni* patients..........El Hawy et al., 1993
Low blood copper levels with asymptomatic HIV-1 infection.....Beach et al., 1992;
Graham, 1992; Shor-Posner et al., 1992
Effect of chronic pancreatitis on copper metabolism..........................Braganza et al., 1981
Effect of diabetes on tissue copper levels
Diabetes mellitus (reduced serum copper)..........................Narang & Wangnoo, 1992
Children with Type I diabetes...................Barg & Wasikowa, 1990; Rohn et al., 1993
Diabetic ketotic patients (adults - insulin dependent).........................Faure et al., 1993
Vitamin C supplementation normalizes ceruloplasmin levels in
insulin-dependent diabetes .... Cunningham et al., 1992
Dietary fructose and copper supplementation...............................Rizkalla et al., 1993
Copper and copper-containing organics in patients with kidney diseases
Renal failure (pre-terminal & terminal) .... Schmitt et al., 1993
Superoxide dismutase levels with nephropathy............................Yamada et al., 1992a
Trace element status in dialysis patients...D'Haese et al., 1992
Haemodialysis ....Forêt et al., 1992; Sagawa et al., 1993
Plasmapheresis therapy..Hoskawa & Yoshida, 1992
Copper and copper-containing agents in patients with liver disease (includes gallstones)
Alcohol liver disease..Kisters et al., 1993
Chronic liver disease..Kikkawa et al., 1992
Stones and bile of patients with pigment gallstones................... Koshinaga et al., 1991
Indian childhood cirrhosis... Sethi et al., 1993
Note that Sethi et al. comment that in the 120 cases studied (abstract), "Dietary copper as a source of this raised copper seems unlikely. The most probable cause could be a defect in the metabolism of copper in ICC patients."
Menkes disease and occipital horn syndrome...Danks, 1993

Wilson's disease (and patients with non-Wilsonian disorders)

Wilson's disease.................. Lim & Choo, 1979; Oga et al., 1993; Rossaro et al., 1990

Non-Wilsonian disorders... Wierzbicki et al., 1993

Trace element associations with cardiovascular diseases

Acute myocardial infarction... Amareshwar Singh, 1992

Aortic aneurysms.. Dubick et al., 1991

Atherosclerosis............................... Peltomaa et al., 1992; Pinheiro et al., 1992, 1993

Hypertension and cardio-cerebrovascular diseases.................... Nomiyama et al., 1993

Miscellaneous..................... Gartside & Glueck, 1992; Oster, 1993; Oster et al., 1993; Reuter et al., 1991; Wen et al., 1993

Levels of copper, copper-containing organics or ceruloplasmin in patients with malignant (or non-malignant) growths/disease

Brain tumours .... Jiang et al., 1991; Manjula et al., 1992; Yoshida et al., 1992a, 1993a; Zheng et al., 1992

Breast cancer... Overvad et al., 1993; Schmid et al., 1993b

Cancer of the digestive tract.. Ma & Jiang, 1993

Cervical cancer................................ Arumanayagam et al., 1993; Shiotani et al., 1993

Colorectal cancer .... Gupta et al., 1993

Esophageal cancer... Sha et al., 1993

Gastric carcinoma.. Narang & Wani, 1992

Gastrointestinal and hepatobiliary cancer...................................... Suzuki et al., 1992a

Larynx cancer... Andrzejewska et al., 1992

Lymphoblastic leukemia .... Van Wouwe & Van Weel-Sipman, 1993

Naso-Pharyngeal cancer .... Leung & Cai, 1993

Non-Hodginkin-Lymphomas .... Schmitt et al., 1992

Ovarian tumours... Napolitano et al., 1992

Pediatric malignancies .... Donma et al., 1992

Prostate cancer... Homma et al., 1992b

Miscellaneous... Liu et al., 1991; Mudgal et al., 1991

Copper levels in patients with miscellaneous diseases

Behçet disease... Dogan et al., 1993

Blackfoot disease .... Pan et al., 1993b

Brain diseases and the aging brain..................... Wender et al., 1992; Yang et al., 1991

Chronic pancreatitis.. Hausmann et al., 1993

Chron's disease and ulcerative colitis .... Ringstad et al., 1993

Cystic fibrosis... Várkonyi et al., 1992; Vormann et al., 1992

Dementia (including Alzheimers disease)....................................... Basun et al., 1991; Connor et al., 1993; Corrigan et al., 1991

Inflammatory rheumatic diseases .... Miesel & Zuber, 1993b; Peretz et al., 1993

Parkinson's disease .... Abbott et al., 1992

Peptic ulcer disease .... Powell et al., 1992

Sickle cell anaemia .... Durosinmi et al., 1993; Ojo et al., 1993

I.5 COPPER AND THE RESPONSE OF THE ORGANISM

As copper is an essential metal, a physiological response can be produced by deficiency. As a toxicant at elevated levels of biologically available metal, a physiological response can be produced by an excess of copper. Most organisms operate somewhere between these two extremes, taking up the metal from the environment or food, storing or transferring it to sites of use. Physiological problems can occur during these processes not directly associated with copper but which will affect the metabolism of the metal. References cited in this section of the report deal with all of these possibilities.

Linder (1991) provides a good, recent review of copper nutrition and metabolism. Wilder and Strik (1991) review nutritional disorders caused by abiotic factors, including copper. Hopkin (1993) presents an excellent review of copper in terrestrial isopods ("pillbugs"), commenting on their ability to store excess copper. Prohaska and Failla (1993) discuss the importance of copper in optimal functioning of the immune system and Sorenson (1992a) and Sorenson et al. (1989) report on the use of bioavailable copper complexes in the treatment of radiation and chronic diseases. Mesocosm work often includes not only the response of the organism but also the geochemistry of the metal (e.g. Hong et al., 1992; Qian et al., 1992; Xu et al., 1992a; Zhang et al., 1987). Reviews that include a discussion of the biological effect of metals in pollutants often include mention of copper (e.g. Brown, 1993; Glime, 1992; Hall et al., 1993).

The response of plants to copper depends on the the chemical properties of the soil (e.g. Franco-Vizcaino et al., 1993), including the biological availability of metals whether in soils, fertilizers or pesticides. Recent references dealing with soil copper, nutrient solutions, sprays and fertilizers include:

Nutrient disorders (copper deficiency and excess).................. Gussarsson & Jensén, 1992;
Smith & Vanden Berg, 1992a,b,c; Smith et al., 1992.

Copper in fertilizers .... McLaren & Ritchie, 1993;
Smithson et al., 1993

Use of copper to enhance plant appearance .... Zhu & Li, 1991

Interactions (phosphorous-copper) in copper-containing nutrient mixes............................
Greipsson, 1992; Rhoads et al., 1992; Sheudzhen et al., 1992; Verma et al., 1993

Soil loading capacity for anthropogenic agents .... Chen & Zheng, 1992

Response to metal-containing sludges and coal ash....................About Seeda et al., 1992a;
Kawecki et al., 1991c

Microorganism and plant response to excess metal................................Morel et al., 1991;
Obbard & Jones, 1993a; Ray, 1991; Singh et al., 1992b

Effect of copper on nitrate reduction in water (laboratory) ....Waara, 1992

The role of copper in photsynthesis is varied and not completely understood. The title of the publication by Arellano et al. (1992) "The ambiguous role of Copper in Photosystem II" is appropriate. It indicates the need for continued exmination of the metabolic roles that are important in understanding growth whether with beneficial or detrimental plants, under conditions of copper deficiency or excess. Recent references dealing with copper and photosynthesis include:

Copper-chlorophyll complexes ....Kowalewska et al., 1992

Photosystem II ....Arellano et al., 1992; Barón et al., 1993;
Renger et al., 1993; Yruela et al., 1992, 1993

Detrimental effects on photosynthesis...................................Lidon & Henriques, 1992a,b;
Lidon et al., 1992; Ouzounidou et al., 1993; Stoyanova & Tchakalova, 1993; Tubbing et al., 1993a

Copper deficiency can affect the physiological response of disease- or parasite-infected organisms. In contrast, copper is used in the treatment of a number of conditions and diseases where the control of organism growth is desired. These include the control of plant and animal diseases.

The treatment will effect a response in the treated organisms. The following references discuss some aspect of these responses:

Uses of copper in chemical root pruning.......................................Flanagan & Witte, 1992;
Svenson & Broschat, 1993

Uses of copper to control plant diseases .... Blum & Gabardo, 1993;
Smith & Papacek, 1991

Effects of fungicides and herbicides on plants and non-target organisms ....
Bozsik, 1991a,b; Evans et al., 1992a; Khetmalas et al., 1993; Marchal-Ségault, 1993; Mårtensson, 1992; Moustafa-Mahmoud et al., 1993; Roberts & Berk, 1993; Shukla, 1992; St-Laurent et al., 1992

Disease control in economically important marine organisms....................Noel et al., 1992

Metal stress effects on host-parasitoid or host-predator relationships ....
Ortel et al., 1993; Schruft et al., 1992

Copper deficiency and disease in domestic animals .... Gengelbach et al., 1993;
Stabel et al., 1993

Heavy metal effects on laboratory animals with experimental infection..............................
Borosková et al., 1993

The response produced by copper in cells and whole organisms can be useful, in controlling unwanted growth or organisms. Conversely, it can be detrimental, especially when non-target cells or organisms are involved. Recent references dealing with both useful and detrimental responses of copper are grouped by the type/nature of the cell or organism and the general nature of the response:

Effects of copper on cells

effect of excess copper on liver cells ....Moteelall et al., 1992;
Toussaint & Nederbragt, 1993

copper-related effects useful in the control of abnormal cell growth (e.g. antineoplastic agents)
.... Byrnes et al., 1992; Engleka & Maclag, 1992;
Orupabo et al., 1992; West et al., 1993b; Zhang et al., 1991a

heavy metals and membrane transport processes .... Ross, 1993

Effect of copper on microorganisms (and others) (bacteria, blue-green "algae", fungi, moss)

association of copper with iron in a magnetotactic bacterium ....
Bazylinski et al., 1993

detrimental effect of excess copper on microorganisms useful in degrading undesirable organics
.... Graham & Arnold, 1993; Quensen et al., 1993;
Roth et al., 1992b

copper and anaerobic digestion of activated sludge ....Lin, 1993;
Mehrotra et al., 1993

effect of copper on activity of bacteria ....Hardoyo et al., 1991

copper sensitivity and/or uptake in plant pathogens............. Cha & Cooksey, 1993;
Obata et al., 1992

soil microorganisms and activity.................................. Bååth, 1992; Hattori, 1992;
Zabawski et al., 1990

sewage sludge metal effects on soil microorganisms..
Chander & Brooks, 1991a,b,c, 1993

cyanobacteria (blue-green "algae") ....Lee et al., 1993d; Lukac & Aegerter, 1993;
Shimamori et al., 1993

metabolic activity and tolerance in fungi................Collett, 1992; Ismail et al., 1991

characteristics of moss growing on copper-rich mine soils...........Shaw et al., 1991

effects on gills and respiratory rate.................. Laurén, 1991 (review of the fish gill as a sensitive target for waterborne pollutants); Marek et al., 1991; Mullick & Konar, 1992; Wilson & Taylor, 1993b

toxicity and physiological response .... Heath, 1991; Hickie et al., 1993; Marek et al., 1991; Mullick & Konar, 1992; Wilson & Taylor, 1993b; Zelikoff, 1993

effects on behaviour.......................................Blaxter & Ten Hallers-Tjabbes, 1992

sensitivity of developmental stages.................................. Nakagawa & Ishio, 1991 (sensitivity greatest in embryo stage)

Responses to excess copper by amphibians

toxicity and abnormal growth..... Luo et al., 1993c; Mironova & Andronikov, 1992

physiological responses........... Naitoh & Wassersug, 1992; Skulskii & Lapin, 1992

Beneficial and detrimental responses to copper by domestic animals

fowl - copper-related physiological problems .... Keirs et al., 1991 (possible effect on gizzard lining with higher levels of copper sulfate supplementation); Ward et al., 1993b (reduction of intake of water and food)

sheep - (animals which can be particularly sensitive to copper)

physiological/biochemical responses to excess copper.. Sansinanea et al., 1993

toxic responses to dust from a "Cu plant"................ Bires et al., 1991a,b, 1993

goats - use of molybdenum to treat effects of excess copper....... Wang et al., 1992f

pig - effects of copper supplementation... Dove, 1993b

cattle .... Herd et al., 1993 (reduced food intake with virus-challenged steers fed diet supplemented with copper; effect not present with Cu+S+Mo supplementation)

Responses of laboratory animals to copper (primarily excess copper)

general responses (behavioural/physiological/biochemical)

Deficiency... DiSilvestro & Medeiros, 1992 (low copper intake by postweanling rats produced pathological symptoms and poor resistance to oxidative stress); Hoogeveen et al., 1993 (deficiency alters energy metabolism and body composition); Larsen & Eggum, 1991 (supplementation of rapeseed diet increased haemoglobin levels)

Excess ..... Belcheva et al., 1992; Ogawa et al., 1992; Singh & Junnarkar, 1991

copper deficiency and immunological function .... Tong et al., 1993 (no apparent association under the conditions of the study)

elevated copper and reduced immune response .... Massie et al., 1993; Posino et al., 1991

effects of exposure to copper chloride.............. Talakin et al., 1991a,c (translations of Russian articles - no effect with single contact with metal-containing dust, effects did occur with ingestion; preventative measures - protective covering and use of dust-controlling measures)

effects of exposure to copper conductor paste (PM-0701) ...... Talakin et al., 1991b (translation of Russian article - toxic effects occurred with ingestion; preventative measures - protective clothing and use of exhaust hoods)

interactions of dietary tin, copper and carbohydrate.................... Rader et al., 1991

miscellaneous.. van den Berg et al., 1993a

References primarily concerned with bioassay organisms or techniques (these references are also discussed or listed in the section on organisms as indicators)

microorganisms as indicators of environmental health .... Ramaiah & Chandramohan, 1993

ecotoxicological impacts of chemicals to multispecies microcosm ..... Sugiura, 1992 toxicity of heavy metals in wastewater to a microorganism (Escherichia coli) used in a bioassay kit (MetPAD) .... Bittori et al., 1992b

equipment useful in environmental/toxicological evaluations.................... Mason & Storms, 1993 (utility of directly coupled size-exclusion high-performance liquid chromatography inductively-coupled-plasma mass spectroscopy to quantify environmentally-induced perturbations in organism metal distribution.

problems and answers in analyzing data from toxicity tests...... Nyholm et al., 1992; Ryan et al., 1992

detrimental effect of antifouling paint metals (Sn, Cu, Zn) on bioluminescence in marine dinoflagellates... Lapota et al., 1993

lichens - detrimental effect of and tolerance to heavy metals................ Garty, 1992

toxicity of copper sulfate to two bioassay crustaceans.......................Gautam, 1990

trace metal toxicity to mitochondrial electron transfer........... Bragadin et al., 1992; Sokol et al., 1991

detrimental effect of copper sulfate on rabbit cellular adenosine triphosphate......... Ogawa et al., 1992

Effect of environmental factors on metal impact

pH effects on growth of microorganisms...................................... Iivanainen, 1993

importance of organic substrate to hydrothermal vent bacteria .... Jannasch et al., 1992

combined effects of pH and organic matter on metal toxicity to bacteria, fungi and phytoplankton.....................................Bagy et al., 1991; Chao & Chen, 1991; Gensemer et al., 1993

effects of calcium on ameliorating copper toxicity -

phytotoxicity in citrus .... Alva et al., 1993

Atlantic salmon... Bjerselius et al., 1993

Several recent references discuss the responses of organisms to industrial emissions or, for humans, the workplace environment. These include organisms found in the field (F), laboratory organisms/conditions (L), bioassay organisms (B) and humans (H):

Metal in coal mine effluents or dusts (F/L/B)....................................... Launer et al., 1992; Trzeciak et al., 1992; Whippler & Dunson, 1993

Plants growing on copper-rich ore bodies or mine spoils (F/L)........... Lanaras et al., 1993; Whiteley & Williams, 1993

Copper processing/production (F/L/B/H) .... Axelson et al., 1983; Hirano et al., 1993; Hosovski et al., 1992; Jop et al., 1991; Karjalainen et al., 1992; Makeev et al., 1992; Miszalski & Niewiadomska, 1993; Wozny et al., 1992; Zhan et al., 1992; Zhu et al., 1992a

Sensitivity to metals in industry (L/H).......... Borosková et al., 1993; Motolese et al., 1993

The responses of cells and organisms to heavy metals such as copper are varied. They include beneficial and detrimental effects (and "no apparent effects" - e.g. Dulin et al., 1992) and deal with morphological, physiological and biochemical processes within cells as well as in organisms. References about effects and responses are grouped according to the general nature of the report.

Requirements for copper

for cell maturation, structure and function....................................... Johnson, 1993; Johnson & Dufault, 1993a; Patrice & Percival, 1993

for normal formation of connective tissue ....Paterson et al., 1993

for immune function............ Paul-Eugène et al., 1992 (effect of copper-substituted bovine lactoferrin); Pocino et al., 1991 (inhibition of immune function with excess

copper); Stevenson et al., 1991 (cattle - they report a lack of effect of single or combined deficiencies of Cu and Se on plasma antibody responses to a challenge)
for normal structure and respiration in mitochondria .... Bode et al., 1992
for normal structure and function of lung cells........................ Akers & Saari, 1993; Richmond & Chi, 1993
as a factor in the new formation of capillaries...................... Alessandri et al., 1983; Lin et al., 1993a; Raju et al., 1984
for normal growth and function of pancreatic acinar cells........... Rao et al., 1993b; Scott et al., 1993
for normal neonatal development of the brain (laboratory animals)........................ Prohaska & Bailey, 1993
copper deficiency and respiratory-distress syndrome (rats).................................... Sarricolea et al., 1993b
Protective effects of copper-containing compounds - cellular photoprotective effect of selenium-copper-vitamin complex .... la Ruche & Césarini, 1991

General responses to excess copper
histopathology in aquatic invertebrates..................... Gardner, 1993 (review article)
abnormal chloroplast structure and function........................... Angelov et al., 1993; Lidon & Henriques, 1993b
enhanced susceptability to photooxidative damage by metals........ Streb et al., 1993
abnormal cells in fish........................ Ahmad & Datta Munshi, 1992; Reimschuessel et al., 1993
abnormal cell growth in laboratory animals .... Suzuki et al., 1991a
inflammation... Mazdai, 1990 (Ph.D. thesis)
inhibition of an amino acid peptide (neurotensin) to pig brain membranes (possibly a result of protein sulfhydryl groups) .... Carraway et al., 1993
adaptative responses (including production of metallothionein-like agents)............ Bassi & Sharma, 1993a,b; Rieger et al., 1993

Effect of copper on lipids and cholesterol
copper and lipid peroxidation
protective effect of copper .... Alberghina et al., 1992; Hamada, 1989
toxic effect of copper... Kadiiska et al., 1993
copper as a possible pro-oxidant.................................... Marzabadi & Jones, 1992
effect of copper deficiency
on lipid peroxide levels in the rat...................................... Tateishi et al., 1992
on composition of membrane lipids in a microorganism....... Peltola et al., 1993
on apolipoprotein synthesis in rat liver cells........................ Reaves et al., 1993
on *in vivo* hepatic fatty acid synthesis........................... Al-Othman et al., 1993
on high density lipoprotein metabolism.................................... Lei et al., 1993
on cholesterol synthesis & release .... Koo et al., 1993
high density lipoproteins and copper-catalyzed oxidation .... Ferretti et al., 1993; Ibdah et al., 1993
low density lipoproteins and copper-mediated oxidation ... Cominacini et al., 1991; Hoff et al., 1992; Retsky et al., 1993; Tamasawa & Takebe, 1992; Zhu et al., 1993
cholesteryl ester hydrolysis.. Tanaka, 1993
inhibition of copper-induced oxidation of low density lipoproteins......................... Chen & Loo, 1993 (effect of cigarette smoke)

effect of excess copper
on degradation of volatile fatty acids in anaerobic digestion..............Lin, 1992
on increasing rate of oxidation in fish oils.............Karahadian & Lindsay, 1989
metal removal-induced increase in oxidation stability of hydrogenated
sunflower oil..Ianov et al., 1992
lipopolysaccharide chemotypes of a microorganism (*Thiobacillus ferrooxidans*) differ between
populations in different mine tailings....................Southam & Beveridge, 1993

The effect of copper on hormones and similar organics
decrease in acetylcholine levels in a clam (*Anodonta cygnea*) .... Salánki et al., 1993
decrease in estrogen activity in a fish (*Cynoscion nebulosus*)..................................
Thomas & Smith, 1993
effect of copper status on luteinizing hormone secretion in dairy steers..................
Xin et al., 1993b (no apparent effect)
reduced catecholamine levels in the neonatal mouse brain......................................
Prohaska & Bailey, 1993
effect of estradiol on induction of copper deficiency.................Koo & Yang, 1993

Copper and its effect on miscellaneous organics and tissues
effect on citric acid formaation by *Aspergillus niger*.............. Honecker et al., 1992
changes in the nature and effect of metabolites..................... Nakayama et al., 1992
microorganism degradation of organics.......................Joshi-Tope & Francis, 1993;
Tatara et al., 1993
dietary copper deficiency induced inhibition of heat shock protein expression.........
Blake et al., 1993
nature of excess copper-induced protein in *Vibrio alginolyticus*.............................
Sayyar et al., 1993
changes in protein or peptide/dipeptide synthesis, nature or content with added
copper ....Cicik & Erdem, 1992; Decker et al., 1992; Lidon et al., 1993c;
Miller et al., 1992; Miyazawa et al., 1992; Shah et al., 1992; Zou et al., 1992b
effect of copper and an alkaloid on bile composition and excretion rate in sheepDeol et al.,
1992
effect on human fibroblast growth factor activity.............Engleka & Maciag, 1992
effect on connective tissue ....Fife et al., 1992; Parry et al., 1993;
Paterson et al., 1993

The effect of copper on enzyme activity
general discussions of enzyme activity and metals (including copper) ....
Bakardjieva, 1986; Fujimoto et al., 1993; Kohen et al., 1992; Pawlicki et al., 1990
(enzyme activity in circadian and seasonal cycles); Wielgus-Serafinska et al., 1990
(enzyme activity in circadian and seasonal cycles)
enzyme activation by copper..........................Ensign et al., 1993 (monooxygenase)
change in activity caused by copper deficiency......DiSilvestro et al., 1992 (Cu-,Zn-
superoxide dismutase (SOD)); Johnson & Dufault, 1991 (protein kinase); Lai et al., 1993
(SOD); Morin et al., 1993 (SOD); Onyezili & Harris, 1993 (catechol oxidase)
increase in activity with added copper............................Grzywnowicz et al., 1993
(increase and then decrease in peroxidase activity); Romandini et al., 1992 (SOD);
Stefanelli et al., 1992
reduction in activity with excess copper............Birinci & Keha, 1992 (note that no
generalization could be made about effect of metals); Fortin et al., 1993 (dopamine-β-

hydroxylase); Freundt & Ibrahim, 1992 (glutathione S-transferase); Gastaldi et al., 1993 (alcohol dehydrogenase); Hyodo et al., 1993 (an oxidase); Johnson et al., 1993c (cytochrome c oxidase); Kanazawa et al., 1993 (interaction of copper and ascorbic acid, on papain activity); Min & Park, 1991 (ATPase); Monod et al., 1993 (metalloprotease); Munshi et al., 1993 (lipase); Pasqualini et al., 1992 (phosphatase); Porter & Austin, 1993 (cytosine deaminase); Robertson & Villafanca, 1993 (CTP synthetase); Sasamoto et al., 1992 (glucose oxidase); Serrano, 1992 (a dehydrogenase); Streb et al., 1993 (catalase); Webster & Kemp, 1993 (protease); Weckx et al., 1993; Wee & Grogan, 1993 (a hydrolase)

effect of modification of copper-containing active site on copper-containing enzymes...Riley, 1993 (tyrosinase)

effect of trace element fertilizers on activity of "soil enzymes"................................ Sheudzhen et al., 1991b

Copper and neural responses

emetic effects of copper sulfate.. Fukui et al., 1993

effect of copper on neuron membrane excitability......................Salánki et al., 1991

effect of metals on gating of current in neurons.............Talukder & Harrison, 1993

copper as an inhibitor of neural response.....................................Araki et al., 1993 (indicators of copper and zinc absorption were inversely related to radial nerve conduction velocities in gun metal foundry workers); Myers et al., 1993c

Copper and cardiovascular problems

copper sulfate supplementation associated with a decrease in serum cholesterol in rats with experimental atherosclerosis....................................Vlad et al., 1993

effect of copper deficiency on cholesterol synthesis & release........ Koo et al., 1993

Involvement of copper in hepatic and urogenital systems

copper and Wilson's disease............Sokol et al., 1992 (increased lipid peroxidation infers that copper hepatotoxicity is associated with radical damage to mitochondria)

copper and childhood liver cirrhosis..Eife et al., 1991 (provide information on infants exhibiting liver cirrhosis, suggest that the disease is a result of copper intoxication but admit that other factors may contribute)

copper and the macular mutant mouse (animal model of Menkes' kinky-hair disease)..................................... Nakagawa et al., 1993a; Shiraishi et al., 1993

interactions of divalent metal ions with bile components.............Saida et al., 1993; Zuman et al., 1993

copper and gall/bile stones.........................Koshinaga et al., 1991; Li et al., 1993d; Ruíz de Aguiar et al., 1992; Shen et al., 1993a

copper and kidney stones... Rodgers et al., 1993

copper and urinary calculi...Küpeli et al., 1993

copper deficiency contributes to silica urolith formation in rats fed high levels of absorbable silica... Stewart et al., 1993

Involvement of copper in genetic material

copper deficiency effects............................. Adachi et al., 1993; Sakai et al., 1993a

copper concentration and nucleic acid concentrations........... Bozhkov et al., 1991; Liashenko et al., 1991; Saint-Jacques & Séguin, 1993 (increased metallothionein mRNA in liver of an amphibian)

metal-responsive gene expression... Quinn et al., 1993
elevated ionic metal and transcription..... Huckle et al., 1993; Takahashi et al., 1992
acid RNAse activity increase with increased Cu in rice............................. Lidon & Henriques, 1993a
copper and DNA damage.................. Chen et al., 1990b; Hashimoto & Nakamura, 1992; Hashimoto et al., 1992a; Hirai et al., 1991; John & Douglas, 1993; Kungolos & Aoyama, 1992; Li & Trush, 1993a; Lloyd et al., 1992; Millard & Hopkins, 1993; Milne et al., 1993; Naseem et al., 1993; Sahu & Gray, 1993; Said Ahmad et al., 1992; Tkeshelasvili et al., 1992; Yamamoto et al., 1993; Zaidi & Hadi, 1992
miscellaneous, copper-related effects..... Akman et al., 1992a,b; Chen et al., 1993d; Chiu et al., 1993; Lesser & Guthrie, 1993

Copper and organism/cell responses to drugs and drug-like agents
copper and drugs used to model physiological/biochemical processes in invertebrates, laboratory animals and humans.. Ireland, 1993; Medeiros et al., 1992; Rodriguez-Montelongo et al., 1993
chemical compounds and the immune system of aquaculture fishes........................ Isayeva & Kozinenko, 1992 (review article)
traditional medicines..... Goel et al., 1992 (tamrabhasma, a copper oxide-containing Indian preparation with anti-ulcer activity may be useful against inflammatory bowel disease)
copper as an anti-inflammatory agent....................................... Franco et al., 1992; Mazdai, 1990 (Ph.D. thesis)
metal interaction with antitetanous vaccination.................. Poupon et al., 1992 (no apparent relationship of copper with immune response)
anti-ulcer activity of copper complexes.... El-Saadani et al., 1993; Goel et al., 1992
with antirheumatoid drugs .... Hashimoto & Lipsky, 1993
with antitumour drugs............................... Barni et al., 1992; Hampton et al., 1993 (discuss mechanisms of action of copper-containing photosensitizer)
role of copper in the toxicity of a thiol-containing radioprotector.......................... Held & Biaglow, 1993
Toxic effects of copper-containing drugs .... Kayahara et al., 1991

Miscellaneous references providing direct or indirect information on the effects of copper
total and leachable metals in zebra mussels from Lake Erie...... Doherty et al., 1993
metal levels in smokeless tobacco and their possible involvement in carcinogenesis and mutagenesis .... Maier et al., 1993
abnormal systemic responses to copper necklaces or bracelets....... Downey, 1992b
metal in diathermy instruments as possible cause of post-surgical granulomatous inflammation in humans .... Henry et al., 1993a
esophageal ulcer produced by ingestion of melted copper......... Shibuya et al., 1992

I.5.1 Copper in dental work

Copper is widely used in dental amalgams in what are classified as "low-cu amalgams" and "high-Cu amalgams" (Marshall and Marshall, 1992). The authors comment that there is increasing use of high-Cu amalgams because of the reduced level of the corrosion-prone phase (g_2) found in low-Cu amalgams. This is associated with improved clinical performance in terms of the marginal integrity of the amalgam (Marek, 1992; Marshall and Marshall, 1992). Some release of copper from amalgams can be beneficial, as a growth inhibitor against oral bacteria (e.g. Drake et al., 1993) although there is evidence of potential cytotoxic effect, at least with orthodontic appliances (Grimsdottir and Hensten-Pettersen, 1992). Some individuals also exhibit an abnormal response to copper (e.g. Downey, 1992a,b) which should be considered with the use of metal-containing dental materials. Recent references that include information on the use or effect of copper in dental work include:

Reviews of dental amalgams...................................Lucas & Lemons, 1992; Marek, 1992; Marshall & Marshall, 1992

Amalgam inhibition of oral bacteria ....Drake et al., 1993; Grimsdottir & Hensten-Pettersen, 1992

Detrimental effects of dental materials... Downey, 1992a; Grimsdottir & Hensten-Pettersen, 1992; Sano & Takeda, 1992

Types and properties of copper-containing dental materials...........Drummond et al., 1992; Hadavi et al., 1992; Johansson & Lagerlöf, 1992; Johnson & Powell, 1992; Kim et al., 1992; Torgersen & Gjerdet, 1992 (metal release from arch bars used in maxillofacial surgery); Veronesi et al., 1992; Wagner et al., 1993; Wataha et al., 1992

Clinical performance of amalgams .... Osborne et al., 1993; Taylor et al., 1993a; Torstenson & Brännström, 1992; Wallman et al., 1992 (report copper release from high-Cu amalgam but note low Cu ion activity due to complexation)

Corrosion and tooth reactions to dental materials ....Günday & Gencoglu, 1992; Holland, 1992; Klinge, 1993; Lucas & Lemons, 1992

I.5.2 BIOLOGY AND COPPER CORROSION

Corrosion resistance is one of the reasons why copper and copper-based alloys are so widely used. Corrosion does occur, however, and can be affected by the chemical nature of the medium as well as the activity of some microorganisms that are often found on the surface of the metal. Pitting corrosion is one of the major concerns in domestic drinking-water installations (reviewed in Wagner, 1992). Corrosion can also cause the release of copper, a factor of some concern to those worried about the level of total copper in the environment. The following references were selected because they relate to "biology and copper corrosion", biofilms or corrosion release of copper:

Factors affecting the rate of corrosion ....Al-Hajji & Reda, 1993; Bozack & Beshears, 1993; Palraj et al., 1991 (galvanic corrosion behaviour, a result of metal-metal interaction and biofilms); Shibad et al., 1989

The nature of corrosion and corrosion films on copper surfaces....................................... Dzierzewicz et al., 1992/1993; Gouda et al., 1993; Little et al., 1993; Nord et al., 1993 (spionkopite as a corrosion product on a copper alloy compass ring from a shipwreck dated 1676); Walker et al., 1993; Zanoni et al., 1992

Corrosion in copper tubing used in drinking water systems.. Angell & Chamberlain, 1993 (*Pseudomonas* isolated from failed pipes with a characteristic pitting); Wagner, 1992 (review of internal corrosion in various tubing types in domestic drinking-water installations)

The biological effect of corrosion-released copper..........Dzierzewicz et al., 1992 (possible beneficial effect, against sulfate reducing, corrosive bacteria)

I.5.3 COPPER IN BIRTH-CONTROL DEVICES

Copper-containing intrauterine devices are one of the several birth-control devices in wide-spread use (e.g. Luukkainen, 1992). Koch et al. (1991) comment that:

> "Copper intra-uterine devices (Cu-IUD's) are a reliable, frequently used, reversible contraceptive method. The rate of failure of Cu-IUD's having a copper surface of $\geq 350\ mm^2$ is distinctly less than 1 pregnancy in 100 women per year. Young women nulliparity is no longer considered to be an unrestricted contraindication. Cu-IUD's can also be used for women with diabetes, renal or oncological diseases and treatment with anticoagulants. Cu-IUD's are devoid of carcinogenic risk, are not casually responsible for ascending infections and extra-uterine pregnancy and don't impair fertility."

Bergsjø (1992) and Fraser (1992) provide general discussions of intrauterine contraceptive devices, pointing out some of the benefits and problems that they provide. As an example of the benefits, Parazzini et al. (1992) provide evidence that gives some support to the suggestion that IUD use may reduce the risk of invasive cervical cancer. Recent references that include discussions of intrauterine devices include:

Uses of contraceptive devices...................... Brosens et al., 1991; Edelman & Porter, 1993

Evaluations of copper-containing devices.................Bozzini et al., 1991; Chi, 1991, 1992; Díaz et al., 1992a,b, 1993; Kimmerle et al., 1993; Ladipo et al., 1991; Piening, 1991; Sivin et al., 1991a,b, 1993; Tiwari & Angra, 1991; van Dierendonck et al., 1992; Wagatsuma et al., 1992; Wang et al., 1992a

Benefits and problems of IUD use........................Amla et al., 1993; Parazzini et al., 1992; Parra et al., 1991; Yin et al., 1993; Zhu et al., 1991a

Copper loss from IUD devices................................Chantler et al., 1992; Kjær et al., 1993; Tsong & Nash, 1991

I.5.4 COPPER AS AN ANTIFOULING AGENT

Copper and copper-containing coatings are widely used to control the growth of unwanted organisms on structures in aquatic environments. References concern both the technology of fouling control and the real and potential impacts of antifoulants (e.g. Bowers-Irons et al., 1990; Great Britain, Department of the Environment, 1992; U.S. National Technical Information Service, 1993f). Recent references can be grouped in the following categories:

Impact of fouling organisms..........................Karande et al., 1993 (timber deterioration by the gribble, *Limnoria platycauda*, including attack on chromated copper arsenate treated timbers)

Patent documents describing new antifouling agents............................ Atsumi et al., 1992 (microbicidal ceramics containing water-soluble salts of Ag, Cu, Zn); Kakehashi, 1992 (elastomeres containing Cu_2O)

Evaluation of methods for protecting underwater structures .... Peterson et al., 1993 (use of the antibiotic tetracycline in copper-bottom paint); Rao et al., 1993c

Biological effect of antifouling agents................................Gibbs, 1993 (evidence of some metal enrichment in bottom sediments near a ship repair facility in Townsville Harbor, Australia); Nell & Chvojka, 1992 (evidence of additive effect of bis-tributyltin oxide and copper on copper accumulation in two species of oysters); Batley et al., 1992 (support of Nell & Chvojka finding, with reduced tissue copper levels after banning tributyl tin use); Peterson et al., 1993; Takano & Hattori, 1992; Weis & Weis, 1993 (found elevated tissue levels of copper in oysters from a CCA-treated bulkhead; report trophic transfer to predatory snails)

I.5.5 COPPER AS A WOOD PRESERVATIVE IN TERRESTRIAL ENVIRONMENTS

Deterioration of wood occurs as a result of fungal, borer, termite and carpenter ant atack. Preservative treatment of the wood will reduce the rate of detrioration. Copper-based agents such as chromated copper arsenate (CCA) are widely used as wood preservatives. Recent literature contains references that discuss the technology as well as the real or potential environmental impact arising from the use of preservatives. Recent literature containing discussions of the use of copper include:

New types of preservatives...Kumar et al., 1991

Effect of wood types/products and wood chemistry on the use of preservatives................
Baecker et al., 1991; Kumar & Dobriyal, 1992; Slabbert, 1992; Vick & Kuster, 1992

Nature and effectiveness of treatment.......................Lee et al., 1993a; McLaughlan, 1991; Ruddick, 1992; Vick & Christiansen, 1993

Toxicity of chromated copper arsenate............................. Cox, 1991 (discusses toxicity of copper, impacts of preservative on non-target organisms and on humans)

Minimizing the effects of copper-containing wood preservatives.......................................
Hirata et al., 1993 (protocol for minimizing gaseous toxicants from burning CCA-treated wood); Pohlandt et al., 1993 (discussion of metal-containing leachates in ash from burned wood that had been preservative treated)

I.5.6 COPPER AS A BIOCIDAL AGENT

Details of the benefits of copper when used in the control of pest organisms, are provided elsewhere in this review. This section provides recent references that consider organism-related effects of copper when used as a biocidal agent. These references are grouped according to the use of the agent:

Bactericides and their effect on target and non-target organisms.......................................
Aplincourt et al., 1992; Chohan & Kausar, 1992; Donegan et al., 1991(physical and chemical control of released microorganisms); Kokosková, 1992; Sobiczewski & Berczynski, 1990; Washington, 1991

Algaecides - tolerance and effect on target and non-target organisms................................
Haglund & Pedersén, 1993; Swain & Adhikary, 1991;

Control of lichens................................ Martin et al., 1992 (copper-containing compounds provided the only effective control over lichens on asbestos cement roofing)

Fungicides and their effect on target and non-target organisms...
Anandaraj & Sarma, 1991; Anderson & Wicks, 1993; Beresford, 1992; Camoni et al., 1991; Dethe et al., 1993; Gomez, 1991; Hseu & Hsu, 1991; Koomen et al., 1993; Laker & Ram, 1992; Mathur & Sobti, 1993; Nene & Thapliyal, 1993 (review of fungicides in plant disease control); Nogueira, 1991; O'Brien, 1992; Patel & Patel, 1992; Ray, 1991; Redl, 1993; Schruft et al., 1992 (effects of fungicides on a useful, predaceous mite); Sharma, 1992; Soyez, 1992a

Herbicides and their effect on target and non-target organisms..
St-Laurent et al., 1992

Molluscicides and other mollusc-controlling agents containing copper..............................
Symondson, 1993 (use of copper strips to confine slugs)

Parasiticides, their use and misuse .... Straus, 1993 (copper sulfate use to control an ectoparasite infestation on catfish fingerlings)

Miscellaneous..............................Alva, 1993 (effect of long-term use of copper sulfate on soils and Hamlin orange trees); Alva et al., 1993 (use of calcium to ameliorate effect of excess copper on citrus trees); Mårtensson, 1993 (effect of pesticides on soil biological processes); Neary et al., 1993 (fate and effects of pesticides in southern forests); Olaofe et al., 1993 (effect of nematicides on cowpea seeds); Parshad et al., 1993 (use of a copper oxychloride fungicide as a repellent for house rats); Yamada et al., 1992b (method for determination of oxine-Cu fungicide in environmental waters)

I.6 COPPER AND THE PHYSIOLOGICAL STATE OF ORGANISMS

The uptake and proper utilization of copper is essential for life. However, the nature of both the uptake and utilization is dependent on the nature of the organism. Although this infers that abnormal physiological conditions will also be unique to the nature of the organism, there are some common trends which allow reference material to be grouped under common headings.

General reviews of the physiological roles and effects of copper .... Alfrey, 1992
(discussion of essential trace elements in humans)

Copper and inflammation
- Copper or copper-containing organics and oxidative stress .... Miesel & Zuber, 1993a; Natesha et al., 1992
- Metal-metal interactions in inflammation .... Tarp et al., 1991
- Copper deficiency and antiinflammatory activity of aspirin .... Kishore et al., 1993

Effects of copper on immunity
- Copper deficiency and immune function .... Prohaska & Lukasewycz, 1990
- Metal pollution and immunodilution .... Zelikoff, 1993

Distribution of copper in connective tissue .... Vittur et al., 1992
- Dietary copper and connective tissue development .... Andon et al., 1992 (evidence that suboptimal intakes of Cu and Mn may increase risk of low bone mass in later life); McCoy et al., 1993 (rat femurs of deficient animals had lower copper levels than those of copper supplemented animals); Ott & Asquith, 1993 (Zn and Cu supplementation of weanling foals did not increase bone mineral deposition rates)
- Postmenopausal bone loss and osteoporosis .... Howard et al., 1992 (low serum copper, a risk factor additional to low dietary calcium in postmenopausal bone loss); Saltman, 1992 (and Saltman et al., 1993 - recommendations for adequate dietary calcium and trace minerals for women at osteoporotic risk)
- Bone-related problems .... Nii et al., 1991; Yasufuku et al., 1991 (periosteal hyperostosis cases with copper deficiency)
- Miscellaneous .... Ohshima et al., 1993

Copper and enzyme activity
- Copper-containing enzymes .... Anonymous, 1993; de Lustig et al., 1993; Ishikawa et al., 1993b; Itoh et al., 1992; Kondo et al., 1992; Kong & Fanburg, 1992; Manzano et al., 1993; Orr & Sohal, 1993; Takahashi & Taniguchi, 1993; Tamura, 1993; Woodruff, 1993
- The effect of copper deficiency .... Johnson & Dufault, 1991, 1993b; Kim & Allen, 1993; Kirkova et al., 1992a,b; Kosonen et al., 1993; Olin et al., 1993; Prohaska et al., 1993
- The effect of excess copper........Andreeva & Okorokov, 1993; Brown et al., 1991; Craik et al., 1992; Kundt & Wilson, 1993; Leung et al., 1992; Lidon & Henriques, 1993a; Lister et al., 1993; Munshi et al., 1993
- Miscellaneous .... Hirota et al., 1993

Liver disorders
- General reviews/discussions........... Blincoe, 1993c (computer simulation of normal and pathological copper metabolism in humans); Brewer, 1992; Fazzin et al., 1987 (use of after meal biliary salt and copper-ceruloplasmn tests to evaluate liver function)
- Animal and cell models of liver disorders .... Abe et al., 1993a; Baba, 1992; Fuentealba et al., 1993; Fujii et al., 1993; Kodama et al., 1993; Koropatnick & Cherian, 1993; Kuipers et al., 1993; Myers et al., 1993a,b; Nakagawa et al., 1993b,c,d; Sato et al.,

1993; Satoh et al., 1991; Schilsky et al., 1993; Seo, 1991 (Ph.D. thesis); Shiraishi et al., 1993; Sokol et al., 1992, 1993a,b; Sugawara et al., 1992a,b, 1993; Takikawa et al., 1991; Tanaka et al., 1993a; Yamada et al., 1993a; Yamate & Tsuji, 1992

Cirrhosis........................ Valencia et al., 1993 (note that "Wilson's disease and ICC cannot be completely separate and both conditions exhibit striking morphologic similarities. It is possible that both entities share a common pathogenic mechanism.")

Copper toxicosis (model of Wilson's disease)............................Brewer et al., 1992 (use of ^{64}copper measurements to diagnose canine copper toxicosis); Haywood & Hall, 1992 (Bedlington terriers); Yuzbasiyan-Gurkan et al., 1993

Wilson's disease - an inherited error of copper metabolism associated with the accumulation of copper in the liver and certain other organs -

General discussions.................................Barlas et al., 1993; Bhave et al., 1994; Borda et al., 1992; Chu & Hung, 1993 (geographic variations in the disease); Miki et al., 1992 (involvement of metals in the pathogenesis of the disease); Sallie et al., 1992 (problems with diagnostic techniques); Stevens & Chopra, 1993 (review)

Diagnosis and disease-related physiological problems.........Bakshi & Pardiwala, 1992; Blasco et al., 1992; Brodland & Bartley, 1992; Gwirtsman et al., 1993; Laufer et al., 1992; Lim & Choo, 1979 (older reference describing the diagnosis of the disease in a 2 year old child); Magnanimi et al., 1991; Mizutani et al., 1990a; Mulder et al., 1992 (metallothionein concentrations in the liver of patients with Wilson's disease, primary biliary cirrhosis and liver metastasis of colorectal cancer); Oga et al., 1993; Shkal'ts et al., 1991; Steindl et al., 1993

Disease treatment and associated problems... Brewer et al., 1993a (use of vegetarian diet to decrease copper bioavailability in food), 1993b; D'Inca et al., 1992; Kiechl et al., 1992; Kiss et al., 1992; Menara et al., 1992; Morita et al., 1992; Rossaro et al., 1990; Zancan et al., 1990

References dealing with the genetic aspects of Wilson's disease......................... Bull et al., 1993; Chelly & Monaco, 1993; Houwen et al., 1993; Petrukhin et al., 1993; Sallie et al., 1993; Tanzi et al., 1993; Thomas et al., 1992

Menkes disease - an inherited disorder of copper metabolism associated with low serum copper levels and impaired incorpporation of copper into enzymes. Characteristics are expressed as neurologic degeneration and mental retardation, connective tissue and vascular defects, brittle and depigmented hair and death in early childhood.

Reviews of Menkes disease and copper metabolism........................Danks, 1993 (disorders of copper transport: Menkes disease and the occipital horn syndrome); Hamer, 1993; Kodama, 1993

Cell growth and metabolism in human and mottled mouse model of Menkes disease ....Gacheru et al., 1993; Kodama, 1993; Rayner & Suzuki, 1992

Disease-related physiological problems...................................Yagi et al., 1991; Yoshimura et al., 1992 (skeletal abnormalities in occipital horn syndrome, an allelic mutation of Menkes disease)

Disease treatment and associated problems.........................Kaler & Gahl, 1992; Kaler et al., 1993; Nakamota et al., 1992; Sarkar et al., 1993

References dealing with the genetic aspects of Menkes disease......................... Chelly et al., 1993; Horn et al., 1992; Kaler & Gahl, 1993; Vulpe et al., 1993

Childhood Cirrhosis - a rapidly progressive hepatic disorder associated with extremely high concentrations of copper within the liver and a number of other characteristics. Often termed "Indian Childhood Cirrhosis" because of the similarities to conditions first described for children in India (see discussion in Bhave et al., 1992). Details of the disease are controversial, as indicated in the article review by Bhusnurmath (1992) and the reply by Gahl et al. (1992). Ramakrishna et al. (1993) note that there are several diseases with similar characteristics. Also controversial are the reported causes of the disease. Eife et al. (1991 and elsewhere) ascribe Childhood Cirrhosis to copper intoxication via tap water while Sethi et al. (1993) comment that, for 120 cases of Indian Childhood Cirrhosis (ICC), (summary) "The most probable cause could be a defect in the metabolism of copper in ICC patients." Bhave et al. (1992) and Morris and Tanner (1993) suggest that there may also be synergistic factors ("toxins") affecting the expression of ICC and other similar diseases. There is obviously a need for uniform criteria for diagnosis (e.g. Bhusnurmath, 1992) to permit a valid explanation for the cause(s) of the disease.

Discussions of cases................................. Aljajeh et al., 1994; Eife et al., 1991; Gaida & Radtke, 1990b; Ramakrishna et al., 1993

Diagnostic Characteristics........................Bhusnurmath, 1992; Gahl et al., 1992

Causes of Childhood Cirrhosis .... Bhave et al., 1992; Eife et al., 1991; Gaide & Radtke, 1990b; Sethi et al., 1993

Miscellaneous... Grases et al., 1993 (lack of obvious relationship between zinc and copper on one group of urinary concretions); Gregorio & Mieli-Vergani, 1993 (urinary copper excretion after penicillamine challenge in chldren with prolonged hepatitis A infection); Iwakawa et al., 1993 (sibling cases of a degenerative neurological disease associated with hypocupraemia and hypobetalipoproteinaemia); Sokol et al., 1992 (role of free radicals in copper hepatotoxicity); van den Ingh & Rothuizen, 1992 (abnormal accumulation in the liver of a boxer dog); Wang et al., 1992f (use of trithiomolybdate to treat copper poisoning); Wierzbicki et al., 1993 (copper metabolism in two patients with non-Wilsonian low copper movement disorders).

Cardiovascular conditions and copper - abnormal levels of copper are often associated with irregular cardiovascular conditions. A number of papers address cholesterol, lipids or arteriosclerosis. The following references provide information on the variety of cardiovascular (or related) conditions affected by, or affecting the metabolic effect of copper.

General reviews..................Allen & Klevay, 1994 (Copper: an antioxidant nutrient for cardiovascular health); Meissner, 1991 (copper is suggested as the most important trace metal in ischemic heart diseases); Powell & Tortolani, 1992 (the role of reactive oxygene intermediates in ischemic injury)

Disease characteristics and the importance of copper or copper-containing organics...Allen & Saari, 1993; Becker et al., 1993; Chao et al., 1993; Chevion et al., 1993; Davidson et al., 1993a; Durak et al., 1993; Fields et al, 1993b; Matz et al., 1993; Medeiros et al., 1991, 1993a,c; Megaw et al., 1993; Nassir et al., 1993; Ohtsuki et al., 1992; Vlad et al., 1993 (copper sulfate reduced edema and lipid infiltration in experimental atherosclerosis); Wahlund et al., 1992

Effect of copper on vascular tissue...................................... Kishimoto et al., 1992 (injury to cultured human vascular endothelial cells by copper sulfate)

Relationship between tissue/serum zinc and copper and cardiovascular diseases ....de Lorgeril et al., 1993; Dubick et al., 1991; Fernández-Britto et al., 1993; Gartside & Glueck, 1993; Oster et al.,, 1993; Salonen et al., 1992; Wen et al., 1993

Relationship between cholesterol and serum trace elements (including copper)....... Abu-El-Zahab et al., 1991

Relationship between copper and lipids and lipoproteins...... Chen & Tappel, 1993; Cominacini et al., 1991; Ding et al., 1993; Ferretti et al., 1993; Ibdah et al., 1993; Kalyanaraman et al., 1991; Lamb et al., 1993; Lindstedt et al., 1993; Lodge et al., 1993; Lynch & Frei, 1993; Mackness et al., 1993; Maiorino et al., 1993; Naruszewica et al., 1992a,b; Nassir et al., 1993; Noguchi et al., 1992, 1993; O'Leary et al., 1993; Olszewski & McCully, 1993; Retsky et al., 1993; Reuter et al., 1991; Sakai et al., 1992; Smith et al., 1993a; Tamasawa & Takebe, 1992; Tanaka & Kanamaru, 1993; Uehara et al., 1990a; Wen et al., 1993; Wieland et al., 1993; Wiseman et al., 1993; Yue et al., 1992; Zhu et al., 1993

Disease treatment and associated problems....... Moat et al., 1993; Williams, 1992a

Miscellaneous diseases - the metabolism of copper is often affected by disease. The nature of many diseases can also be affected by a deficiency or excess of biologically available copper. The following references provide information on a range of diseases that involve the metabolism or effect of copper.

Pancreatitis - evidence of altered copper metabolism.............Braganza et al., 1981

Dietary copper deficiency and the pancreas.................Weaver, 1991 (Ph.D. thesis)

Dietary copper deficiency and abnormal glucose metabolism................................. MacDonald et al., 1991; Saari & Bode, 1993

Diabetes and side effects..........Cochrane & Furth, 1993 (bound lipid and transition metal associations in glycation endproducts); Loven et al., 1992 (copper metabolism and gestational diabetes); McDermott et al., 1993 (dietary carbohydrates and antioxidant status); Ookawara et al., 1992 (release of copper from Cu,Zn-superoxide dismutase by glycation reactions); Wachnik et al., 1992 (hepatic lipid peroxidation and trace elements)

Copper-containing hypoglycemic drugs.........................Hatzidimitriou et al., 1993

Direct and indirect relationships of copper and Parkinson's disease symptoms........ Mizuta and Kuno, 1993; Zhang et al., 1993a

Direct and indirect relationships of copper and amyotrophic lateral sclerosis.......... Rosen et al., 1993

Direct and indirect relationships of copper and aging.................Basun et al., 1991; Vanvleteren, 1993 (oxidative stress and ageing in a nematode laboratory animal); de Lustig et al., 1993 (Cu,Zn-superoxide dismutase activity in red blood cells and serum in demented patients and in aging

Direct and indirect relationships of copper and Alzheimer's disease........................ Basun et al., 1991

Angiogenesis (capillary formation)

Copper effects................................Alessandri et al., 1983 (heparin and copper are important components of the new formation of capillaries); Glade, 1992 (copper deficiency as a cause of defective angiogenesis); Raju et al., 1984

Copper and abnormal cell growth/metabolism

Distribution and concentration of copper in cancerous tissues................................ Schrauzer, 1991; Uchida et al., 1993; Yoshida et al., 1993a

Effect of dietary copper deficiency on tumour development.................................. Schuschke et al., 1992

Role or activity of copper in treating abnormal cell growth (includes copper-containing anticancer drugs..................................Brem et al., 1992; Burdon et al., 1993; Crispens & Sorenson, 1992; Pal et al., 1993b

Miscellaneous................................Gangadharan et al., 1990; Suzuki et al., 1991a; Yoshida et al., 1992b

Environmental effect of anthropogenic metals, including copper

Use of gene frequencies to monitor environmental effect.........Hummel et al., 1991

Miscellaneous

Copper and hormone production..Moephuli et al., 1993

Copper deficiency and respiratory membrane damage............Akers & Saari, 1993

Trace elements and improved adhesion of skin grafts for major burns.....................
Berger et al., 1992a (see also Berger et al., 1992b)

Copper and the effects of nicotine............... Bui et al., 1993 (copper deficiency and nicotine exposure may exacerbate the biochemical events associated with cardiovascular diseases); Mongiat et al., 1992 (slight effect of smoking on ceruloplasmin levels in certain welders)

Toxicology of copper-containing drugs for rheumatoid- and osteo-arthritis............
Kayahara et al., 1991

Physiology/biochemistry of invertebrate organisms................Nonnotte et al., 1993 (copper-related gill damage in a shore crab); Rainer & Brouwer, 1993 (hemocyanin synthesis in the blue crab); Truchot & Boitel, 1992 (excess copper-related effects on hemocyanin action)

Effects of metallothionein and stress-induced proteins............. Ellerby et al., 1993; Farrell et al., 1993; Hahn & Gahl, 1993; Kito et al., 1992; Steinebach & Wolterbeek, 1992b; Yiangou & Papaconstantinou, 1993

I.7 INTERACTIONS OF COPPER WITH ORGANICS

The body of literature characterizing the association between metals and organics continues to grow rapidly (e.g. Hutchens and Yip, 1992; Kohen et al., 1992; Mathews, 1993; Reinecke et al., 1992). Copper is essential to the functioning of biological systems largely because it is a critical component of a large number of important organics (Anonymous, 1992; Chesters and Arthur, 1988; Kitajima, 1992; Pitari et al., 1993; Preisig et al., 1993) and functions as a catalyst in important biochemical reactions (Arellano et al., 1992; Bakardjieva, 1984,1986; Chattopadhyay et al., 1992; Chen et al., 1990a; Engleka and Maciag, 1992; Retsky et al., 1993; Sahbaz and Somer, 1993; Vahcic et al., 1992). Consequently, copper is used, directly and indirectly, in the synthesis of organics by man (Barbas et al., 1993; Craik et al., 1992; Gregory et al., 1993; Kant, 1993; Tucker et al., 1992). The ability of copper to form organic complexes is exploited analytically in the detection and characterization of natural organics (e.g. Lati et al., 1992; Scott et al., 1991; Sigman et al., 1991; Tsai and Weber, 1992; Voulgaropoulos and Tzivanakis, 1992; Wirth et al., 1993); quantification of biocidal agents (e.g. Malik and Rao, 1992); quantification of the metal in solutions (e.g. Shamsipur and Alizadeh, 1992), natural systems (e.g. Hsieh and Liu, 1993; Gayet et al., 1993) and in organisms (e.g. Johnson and Dufault, 1993b); and in the removal of metal ions from solution (e.g Yuan et al., 1992).

As described in an earlier section of this review, the reaction of copper with organics may be detrimental (e.g. Carraway et al., 1993) if the metal is present in excessive amounts **and** if it is in a biologically available form (Held and Biaglow, 1993). Biological availability depends on the speciation of the metal which in turn is affected by a wide range of environmental conditions (e.g. pH, dissolved organic carbon, etc.) (e.g. Bagy et al., 1991; Gensemer et al., 1993; Jackson et al., 1993; Rubio et al., 1991; Tadano et al., 1992; Vangronsveld and Clijsters, 1992) and the geochemical cycling of the metal (Chester, 1988; Gerringa et al., 1991; Halen et al., 1991; Ouddane et al., 1992; Raghupathi and Vasuki, 1992). The picture is further complicated by the production of organic compounds by living organisms as well as their liberation into the environment upon decay (Cabral, 1992; Chao and Chen, 1991; Kratz et al., 1991; Lepp, 1992). Finally, organics of anthropogenic origin may affect the biological availability of copper (e.g. Chander and Brookes, 1991a,d; Grzebisz et al., 1993). The nature and physiology of the organism itself (also under control of various environmental conditions) may determine its response to excess available copper (Bradley et al., 1992; De Vos et al., 1993; Malyarevskaya and Karasina, 1991; Rao and Gowrinathan, 1992; Tubbing et al., 1993b). The complexity of the web of interactions involving copper as well as the dual nature of the metal (both essential and potentially detrimental) make predictions of its potential impact very difficult although projections are improved by studies of its behavior in particular ecosystems (e.g. Elbaz-Poulichet et al., 1990; Karathanasis and Thompson, 1993; Linnik and Osadchaya, 1992; Reczynska-Dutka, 1991)

The range of organics and the recent literature dealing with them are both numerous and diverse. As a result, a very brief introduction of each major group is provided with pertinent references that have recently appeared. The references deal with one or more aspects of the function or chemical structure of chemicals in the group as well as the factors that may affect the function and structure. Many of the publications are also used in discussions found elsewhere in the review.

Copper and enzymes

Cu-,Zn-superoxide dismutase (SOD) is an extremely important antioxidant enzyme which converts superoxide dismutase to the less reactive H_20_2.

Structure, biochemistry - Apella et al., 1993; Ascone et al., 1993; Banci et al., 1993; Bertini et al., 1993; Bolann and Ulvik, 1991; da Silva et al., 1992; Desideri et al., 1993; Djinovic Carugo et al., 1993; Gurbiel et al., 1993a (Ag,Cu-SOD); Hirayama et al., 1993; Kintanar and Chen, 1993; Kröniger et al., 1991; Laihia et al., 1993; Lu et al., 1993; Luo et al., 1993b; Michalski and Prowse, 1991; Milne and Johnson, 1993; Naito et al., 1992; Narimoto et al., 1993 (Review); Niwa et al., 1993; Pan and Yau, 1992; Petkau et al., 1989; Scozzafava and Viezzoli, 1993; Sette et al., 1993; Takahashi and Taniguchi, 1993; Tibell et al., 1993; Vanfleteren, 1993; Willems et al., 1993a;

Genetics - Anonymous, 1993; Barkats et al., 1993; Eggerding and Epstein, 1992; Ellerby et al., 1993; Galiazzo and Labbe-Bois, 1993; Hong et al., 1993b,c; James et al., 1993; Jornot and Junod, 1993; Jow et al., 1993; Lu et al., 1992; Orr and Sohal, 1993; Rosen et al., 1993; Sakamoto and Tanaka, 1992; Sakamoto et al., 1993; Seto, 1990 (Ph. D. Thesis); Sinet and Ceballos-Picot, 1992; Yang et al., 1993;

Localization, actions and physiological activity - Argese et al., 1993; Costanzo et al., 1993; Coursin et al., 1992; Das and Fanburg, 1993; Davies et al., 1993; Favero et al., 1992; Fu et al., 1992; Hong et al., 1993b; Kaler et al., 1991 (human MnSOD binds Cu)**;** Kiyosawa et al., 1993; Kobayashi et al., 1993; Labuda et al., 1991; Liou et al., 1993; Munim et al., 1992; Nishiyama et al., 1991; Nonogaki et al., 1992; Percival, 1993; Percival et al., 1993a; Romandini et al., 1992; Sakai et al., 1993b; Satoh et al., 1993; Shiotani et al., 1991; Sines et al., 1992; Sinet and Ceballos-Picot, 1992; Singh and Kumar, 1993; Steinman, 1993; Tian et al, 1992b, 1993; Voegeli et al., 1993; Yim et al., 1993; Yong, 1991 (Ph. D. Thesis);

Activity or localization under abnormal or deficient conditions - Adachi et al., 1993; Baba, 1992; Barkats et al., 1993; Brown and Strain, 1992; Burdon et al., 1993; Ceballos et al., 1991; Ceballos-Picot et al., 1992; Das and Fanburg, 1993; Davidson et al., 1993b; Daza et al., 1993; de Lustig et al., 1993; Durak et al., 1993; Emerit et al., 1991 (trials using Cu Zn SOD in treatment of Crohn's disease); Faure et al., 1993; Fischer et al., 1993; Gao et al., 1993a; Hausmann et al., 1993; Hérouart et al., 1993; Hoshida et al., 1993; Ishikawa et al., 1993b; Itoh et al., 1992; Keshavarzian et al., 1992; Kikkawa et al., 1992; Kojima et al., 1993; Kong and Fanburg, 1992; Kurosawa et al., 1993; Lai et al., 1993; Ledwozyw, 1991; Lehr et al., 1993; Levieux et al., 1991; Lewis et al., 1992a; Li et al., 1993b; Livingstone et al., 1992; Loven et al., 1992; Manzano et al., 1993; Miesel, 1992a; Nakagawa et al., 1992; Ohara et al., 1992; Ohno et al., 1992a; Ohoi et al., 1993; Ohtsuki et al., 1992; Ookawara et al., 1992; Sarvazyan et al., 1993;

Schrauzer, 1991; Sen Gupta et al., 1993; Sharonov and Churilova, 1992; Shiotani et al., 1993; Siflinger-Birnboim and Malik, 1993; Sun et al., 1993; Suzuki et al., 1993a; Wahlund et al., 1992; Wang et al., 1993f; Yamada et al., 1992a; Zhang et al., 1993a,b;

Other enzymes

Dehydrogenases - Allen and Saari, 1993; Davidson et al., 1993c; Gastaldi et al., 1993; Gayet et al., 1993; Indrati and Ohta, 1993;

Oxidases (including peroxidases) **-** Agrò and Rossi, 1992; Babcock, 1992; Bakardjieva, 1986 (Review of plant peroxidase); Bakardjieva and Christova, 1991; Branchaud et al., 1993; Brown et al., 1991; 1993b,d; Calhoun et al., 1993; Castellano et al., 1993; Chao and Medeiros, 1993; Chen et al., 1990a; Coll et al., 1993; Cooper, 1992; Crinson and Nicholls, 1992; Dake, 1992; Dake and Amemiya,1991, 1992; Davidson et al., 1993b; Day et al., 1993; Dooley, 1993; Esaka, 1993; Fee et al., 1993; Ferrari et al., 1990; Fortin et al., 1993; Gacheru et al., 1993; Gayet et al., 1993; George et al., 1993a; Georgiadis et al., 1993; Gurbiel et al., 1993b; Guzzi and Sportelli, 1992; Hämäläinen et al., 1993; Hill, 1993 (*Bacillus* oxidase lacking a Cu_A site); Hill et al., 1992; Hoff et al., 1992; Hoshi et al., 1993; Hosler et al., 1993; Houen et al., 1993; Ingledew et al., 1993; Inoue and Kato, 1992; Ito et al., 1992; Johnson and Dufault, 1993b; Kelly et al., 1993; Koikeda et al., 1993; Kondo et al., 1992; Krebs and Krawetz, 1993; Kyritsis et al., 1993; Lappalainen et al., 1993; Lee and Holm, 1993; Li, 1992a (Ph. D. Thesis); Libby and Averill, 1992; Malmström and Aasa, 1993; Mather et al., 1993; McCracken et al., 1992; McIntire and Hartmann, 1993; Medeiros et al., 1993b; Messerschmidt et al., 1993; Meunier et al., 1993; Milne and Johnson, 1993; Miyoshi-Akiyama et al., 1993; Moir et al., 1993; Mondovi et al., 1992; Mulryan and Mason, 1992; Mure and Klinman, 1993; Musser et al., 1993; Nanthakumar et al.,1992, 1993; Nasir et al., 1992a; Newman et al., 1993; Nishida et al., 1992; Onyezili and Harris, 1993; Opoku-Gyamfusa et al., 1992; Palmieri et al., 1993; Pan et al., 1993a; Preisig et al., 1993; Saiki et al., 1993; Sayre et al., 1993; Shah et al., 1993; Shahar et al., 1992; Shinmyo et al., 1991; Steffens et al., 1993; Suzuki and Hagiwara, 1993; Takahashi et al., 1993; Takayanagi and Yashiro, 1992; Tamura, 1993; Tarp et al., 1991; Tsubaki and Yoshikawa, 1993a,b; Tsubaki et al., 1993; Turowski et al., 1993; Vianello et al., 1993; Vignevich et al., 1993; Wang and Sayre, 1992; Wang et al., 1993b; Whittaker, 1993; Whittaker and Whittaker, 1993; Wieland et al., 1993; Woodruff, 1993; Yumoto et al., 1993; Zhang et al., 1993c;

Oxygenases **-** Arai et al., 1992; Baldwin et al., 1992; Bhat et al., 1993; Chan et al., 1993; Takase et al., 1992; Tripathi et al., 1992; Wigfield and Goltz, 1993; Zhao et al., 1991

Reductases **-** Abraham et al., 1993; Glockner et al., 1993; Hashimoto et al., 1992b; Kohzuma et al., 1993**;** Mchaourab et al., 1993; Moir et al., 1993; Suzuki et al., 1993b; Ye et al., 1993b

Miscellaneous enzymes - Addison et al., 1992; Bacci, 1993; Brown et al., 1993c; Burstyn and Deal, 1993; Chesters and Arthur, 1988 (Review); Davies et al., 1993; Dzierzewicz et al., 1992; Kundu and Wilson, 1993; Lidon and Henriques, 1993a; Odermatt et al., 1993; Oetting and King, 1993; Pawlicki et al., 1990; Rajendran et al., 1992; Riley, 1993; Siflinger-Birnboim and Malik, 1993; Tagaki et al., 1993; Wielgus-Sarafinska et al., 1990; Youn et al., 1991; Yuan et al., 1993; Zhao et al., 1991;

Inhibition of enzyme activity - Chevalier and Rupp, 1993; Craik et al., 1992; Dreyer et al., 1993; Grzywnowicz et al., 1993; Hashimoto et al., 1992b; Ike et al., 1992; Lind et al., 1993; Lister et al., 1993; McGrath et al., 1993a; Monod et al., 1993; Nok et al., 1993; Pasqualini et al., 1992; Robertson and Villafranca, 1993; Webster and Kemp, 1993

Selected blue-copper proteins - Antholine et al., 1993; Assavanig et al., 1992; Barber et al., 1993; Belford, 1993; Brader et al., 1992; Brischwein et al., 1993; Canters and Gilardi, 1993; Christensen et al., 1992a; Clark and Solomon, 1992; den Blaauwen and Canters, 1993; den Blaauwen et al., 1993; Djebli et al., 1992; Ehrenstein et al., 1993; Farver and Pecht, 1992; Freeman et al., 1993b**;** George et al., 1993b; Germanas et al., 1993; Govindaraju et al., 1993; Haladjian et al., 1993; Hansen et al., 1993; Hunt et al., 1993a; Li and McMillin, 1992; Li et al., 1992d; Mizoguchi et al., 1992; Morpurgo et al., 1993; Murphy et al., 1993; Nunzi et al., 1993; Pascher et al., 1993; Romero et al., 1993; Rydén and Hunt, 1993; Sagi et al., 1993; Sakurai, 1994; Scharf and Englehard, 1993; Semenov et al., 1993; Shadle et al., 1993; Shepard et al., 1993; Van de Kamp et al., 1993;

Plastocyanin and cytochromes - [physiological partners] - "plastocyanin is a 10 kD blue copper protein which is located in the lumen of the thylakoid where it functions as a mobile electron carrier shuttling electrons from cytochrome *f* to P700 in Photosystem I" (Gross, 1993) Christensen et al., 1992b; Dennison et al., 1993; Gross, 1993 (Review); Lowery et al., 1993; Medina et al., 1993; Qin and Kostic, 1993; Zhou and Kostic, 1993; Zhou et al., 1992;

Hemocyanin -Adamska, 1990; Andrew et al., 1993; Baldwin et al., 1992; Boteva et al., 1991, 1993; Engel et al., 1993; Kitajima et al., 1993a; Kitajima et al., 1992b; Rainer and Brouwer, 1993; Tom et al., 1993; Topham et al., 1993

Metal-containing transport agents - the transport of metals, nutrients and gases within an organisms involves organic agents. Copper-containing agents include -

Ceruloplasmin **-**Amareshwar Singh, 1992; Andrzejewska et al., 1992; Aselderova, 1992; Baba, 1992; Bertoni et al., 1991; Borda et al., 1992; Bozic and Gvozdic, 1993; Brown and Strain, 1992; DiSilvestro and Joseph, 1993; Fazzin et al., 1987; Fleming and Gitlin, 1992; Fox and Salvatore, 1992; Goode et al., 1993; Knekt et al., 1992; Kornatowski and Durko, 1992; Kubota et al., 1991; Larsen and Sandström, 1992b; Lee et al., 1993e; Livshits et al., 1992; Mainero et al., 1992; Martinez Lista et al., 1993; McArdle and Spenser, 1993; Milne and Johnson, 1993; Mongiat et al., 1992; Mulryan and Mason, 1992; Musci et al., 1993a; Nakagawa et al., 1993a; Natesha et al., 1992; Stern and Frieden, 1993; Subotzky et al., 1992;

Cupredoxins **-** Loehr, 1992

Transferrins **-** Grossmann et al., 1993

Organics involved in metal buffering, metal mobilization and metal elimination or storage in organisms - the biological availability of copper is controlled by the chemistry of the environment. However, once metal is taken up by an organism the distribution, storage, mobilization and to some extent, the impact, is dictated by a group of organics that have a strong metal-binding ability. The most frequently discussed of these is metallothionein although others (e.g. phytochelatin) are also very important.

General - evidence for regulation of uptake, transport and buffering within the organism/cell - Bérail et al., 1992; Cruz-Ortega and Ownby, 1993; Hayashi et al., 1992; Larsen, 1993; Larsen and Sandström, 1992a; Martoja and Marcaillou, 1993; O'Halloran, 1993; Piccinni, 1989; Piccinni and Albergoni, 1992 (Review); Raspor and Pavicic, 1992; Seo and Ettinger, 1993a,b; Thiele, 1993; Yazgan et al., 1993; Zolotukhina and Gavrilenko, 1992 ;

Phytochelatin **-** Salt, 1989 (Ph. D. thesis); Zeng and Hemmasi, 1992

Metallothionein and metallothionein-like agents **-** Baba, 1992; Bremner, 1991b; Brouwer et al., 1993; Burgess et al., 1993a; Cavallini and Albergoni, 1992; Chan and Cherian, 1993; Cosson, 1992 (Review); Cserjesi et al., 1992; Da Costa Ferreira et al., 1993; Dallinger et al., 1993; Evans et al., 1992b; Falnoga et al., 1991; Freedman et al., 1993; Hahn and Gahl, 1993; Hong et al., 1993a; Huckle et al., 1993; Hunziker, 1991; Hylland et al., 1992; Karin et al., 1993; Kito et al., 1991, 1992; Koropatnick and Cherian, 1993; Lee et al., 1991a, 1993b, 1994; Lerch, 1991; Li, 1991 (Ph. D. Thesis); Matsumoto et al., 1992b,c; Micallef et al., 1992; Mulder et al., 1992; Muller et al., 1993; Narula et al., 1993a,b; Oberleas and Chan, 1991; Okada et al., 1992; Pavicic et al., 1993; Radtke et al., 1993; Richards, 1991b; Ringwood and Brouwer, 1992, 1993; Robinson, 1993; Robinson et al., 1992; Saint-Jacques and Séguin, 1993; Sakurai et al., 1993a; Salt, 1989 (Ph. D. thesis); Sayers et al., 1993; Sayyar et al., 1993; Schlenk et al., 1993; Schmid et al., 1993a,b; Stagg et al., 1992; Steinebach and Wolterbeek, 1992a,b; Stockert et al., 1991; Sugawara et al., 1991, 1992a; Sumi et al., 1993; Suzuki et al., 1990, 1992b; Takatera and Watanabe, 1993; Tamai et al., 1993 (suggest MT may function as antioxidant); Thiele et al., 1992; Thorvaldsen et al., 1993; Weser and Hartmann, 1991; Wesson et al., 1991; Whanger, 1991; Winge, 1991; Witkowska et al., 1991; Wolters et al., 1993; Yamada and Koizumi, 1993; Yoshida et al., 1993c; Zelger et al., 1993; Zhou and Goldsbrough, 1993;

Hormones and hormone-like agents - Bal et al., 1992; Freeman et al., 1993a; Kovacic et al., 1991; Kovaleva et al., 1992; Okabe and Hokaze, 1993; Raju et al., 1984; Ravasio et al., 1993; Ryan et al., 1993

Genetic material - Akman et al., 1992a,b; Baker, 1993; Bashkin et al., 1993; Begum and Manohar, 1992; Bozhkov et al., 1991; Bull et al., 1993; Chelly and Monaco, 1993; Chen et al, 1990b; Chen et al., 1993a,b; Dameron et al., 1993; Douglas et al., 1991; Frank-Kamenetskii et al., 1991; Gao et al., 1993b; Hashimoto and Nakamura, 1992; Hirai et al., 1991; Hudson et al., 1992; Hunt et al., 1993b; John and Douglas, 1993; Li and Trush, 1993a,b; Lim and Cooksey, 1993; Liu et al., 1993; Lloyd et al., 1992; Mazumder et al., 1992; Mazumder et al., 1993a,b; Meadows et al., 1993a,b; Mett et al., 1993; Mills et al., 1993; Milne et al., 1993; Naseem et al., 1993; Nothwang et al., 1992; Okamoto et al., 1991; Polycarpou-Schwarz and Papavassiliou, 1993; Ralston, 1991 (Ph. D. Thesis); Said Ahmad et al., 1992; Scott et al., 1991; Sigman et al., 1991; Stangret and Savoie, 1993; Takahashi et al., 1992; Thiele et al., 1992; Yamamoto et al., 1993; Zhao et al., 1993b**;**

Miscellaneous copper-containing or copper-affected organics - Abu-Ghazaleh et al., 1993; Afanas'ev et al., 1993; Alberghina et al., 1992; Alessandri et al., 1983; Amigó et al., 1992; Arimoto et al., 1993; Arulsamy and Zacharias, 1992; Bagy et al., 1991; Barker and Mauk, 1992; Barluenga et al., 1987; Barón et al., 1993; Barrish et al., 1993;

Barton et al., 1992; Basosi et al., 1992; Blanco and Hynes, 1992; Bolann and Ulvik, 1993 (SOD-like activity); Bontchev et al., 1992; Brooks and Davidson, 1993; Byrnes et al., 1992; Cabral, 1992; Carrier et al., 1992; Cesàro et al., 1988; Chelly et al., 1993; Chen et al., 1992d,e; Chen et al., 1990a; Chiessi et al., 1993; Colaneri and Peisach, 1992; Daniele et al., 1992; Davankov et al., 1993; Dean et al., 1992; Decker et al., 1992; Escandar and Sala, 1992; Fenton, 1992; Furbee et al., 1993; Gajda et al., 1992; Galaev and Mattiasson, 1993; Gasque et al., 1992; Ghirlanda et al., 1993; Gregory et al., 1993; Greiner et al., 1992; Gyurcsik et al., 1992; Han et al., 1991; Hassaan, 1992; Hay et al., 1993; Hoskin et al., 1993; Hsieh and Liu, 1993; Indira et al., 1993; Johnson et al., 1993b; Kaler and Gahl, 1993; Kalyanaraman et al., 1991; Kanai et al., 1992; Karagiannidis et al., 1992; Kitajima et al., 1992a; Kohzuma et al., 1993; Krämer et al., 1993; Krari and Allain, 1993; Krätsmár-Smogrovic et al., 1991; Kreszowski and Babcock, 1993; Kukis et al., 1993; Labuda et al., 1991; Lapcik et al., 1992; La Ruche and Césarini, 1991; Lati et al., 1992; LeCoz and Mann, 1992; Lee, 1991 (Ph. D. thesis); Lekchiri et al., 1991; Liao et al., 1991; Liu et al., 1992; Lodge et al., 1993; Lynch and Frei, 1993; MacNeil and Burton, 1993; Maher et al., 1992; Mann et al., 1992; Massa and Giulivi, 1993; Masuoka et al., 1993; Meagher et al., 1992; Micera et al., 1992; Miyazawa et al., 1992; Miyoshi et al., 1992; Mizutani et al., 1990b; Mohamadou et al., 1992; Mohan et al., 1993; Mokhtar et al., 1991; Morel et al., 1991; Myachina et al., 1991; Nakamura et al., 1992; Nasir et al., 1992b; Nicolás et al., 1993; Nomata et al., 1993; Ochiai et al., 1991; Ochocki et al., 1992; Odani et al., 1992; Olivieri, 1992; Olszewski and McCully, 1993; Ozawa and Hanaki, 1992; Ozawa et al., 1992,1993; Pal and Das, 1992; Pandey et al., 1992; Pandiyan et al., 1992; Papavassiliou, 1993; Peisach et al., 1993; Pickering et al., 1993; Pogni et al., 1993; Predki et al., 1992; Redinbo et al., 1993; Rodriguez Placeres et al., 1992; Roth et al., 1992a; Rüttimann et al., 1992; Salas et al., 1992; Sanaullah et al., 1993; Santiago and Soderquist, 1992; Sarkar et al., 1993; Sarvetnick et al., 1993; Sastry et al., 1992; Scheidt et al., 1993; Scrimin et al., 1992; Schwarz and Stieglitz, 1992; Seo, 1991 (Ph. D. Thesis); Shah et al., 1992; Shakir et al., 1992; Shamsipur and Alizadeh, 1992; Sheppard and Kontoghiorghes, 1993; Shimaoka et al., 1993; Shen et al., 1993a; Sibilia et al., 1993; Sóvágó et al., 1993; Spanenberg et al., 1993; Sparks et al., 1993; Stephan and Scholz, 1993; Suzuki et al., 1992c; Tanaka et al., 1992b; Tsai and Weber, 1992; Tyeklár et al., 1993; Urano et al., 1993; Van den Berg et al., 1993a; Vulpe et al., 1993; Wade et al., 1993; Wang et al., 1992, 1993e; Wapnir et al., 1993; Wathen and Czarnik, 1992; Watmough et al., 1993; Weijnen et al., 1992; Wicks and Findsen, 1993; Wilson et al., 1992; Wirth et al., 1993; Yamagishi et al., 1991; Yang and Yang, 1989, 1992; Yruela et al., 1993; Yukawa, 1992; Zuberbühler, 1991;

Copper-containing organics used to control diseases in plants and animals - Blahová et al., 1992; Böhland et al., 1990; Rao, 1992b; Wang et al., 1992;

Copper and organics in medicine and foods - [including imaging] Aplincourt et al., 1992; Bláhová et al., 1991; Botha et al., 1992; Brem et al., 1992; Cao et al., 1992; Chohan and Kausar, 1992, 1993; Durán et al., 1993; El-Gyar et al., 1992; Fujibayashi et al., 1993b; Ghandour et al., 1992; Goodgame et al., 1992; Green et al., 1991; Hampton et al., 1993; Hassaan, 1992; Hatzidimitriou et al., 1993; Hueso-Ureña et al., 1993; Jezowska-Bojczuk et al., 1993; Kadiiska et al., 1993; Kant, 1993; Kayahara et al., 1991; Khan et al., 1992b; Khodari et al., 1993; Kozlowski et al., 1992; Li and Meares, 1993; Mendoza-Díaz et al., 1993; Miesel, 1992b; Monti et al., 1993; Mukherjea-(Nayak) and Bhattacharyya, 1993; Pal et al., 1993a; Saji et al., 1993; Selman et al., 1993; Sevilla et al., 1992; Sher et al., 1993; Shlyakhovenko et al., 1991; Shoukry, 1992; Sokolík et al., 1992a,b,c; Sordelli et al., 1993; Varadarajan et al., 1992; Varshney et al., 1991; Wolters et al., 1992; Wu and Williams, 1993; Yiangou and Papaconstantinou, 1993; Yourtee et al., 1991; Zarytova et al., 1993;

Naturally-occurring organics that affect the availability or the uptake of copper by organisms - this group includes a wide range of metal-complexing and metal-sorbing organics that occur in natural environments. These are also agents that affect the biological availability of copper.

Humic substances and other, similar soil and water/sediment organics - Alberts et al., 1992; Baydina, 1993; Bunzl and Schimmack, 1991; Dehorter et al., 1992; Finger and Klamberg, 1993; Fleming and Gitlin, 1992; Fukushima et al., 1992; Gamayunov et al., 1991 (mathematical model of ion exchange); Hänninen et al., 1993; Kuiters and Mulder, 1993a; Machado et al., 1993; McKnight, 1991 (Review of feedback mechanisms in aquatic ecosystems); Navrátilová and Kula, 1993; Oden et al., 1993; Porter, 1992; Rate et al., 1992, 1993; Rees, 1991; Sekulic, 1990a,b; 1991; Senesi, 1992 (Review of techniques); Shan and Chen, 1993; Slabbert, 1992; Stevenson et al., 1993; Town and Powell, 1993; Wu et al., 1990; Yu et al., 1991a; Zhou, 1992 (biosorption); Zhou and Banks, 1992 (biosorption); Zyczynska-Baloniak et al., 1991;

Effect on metal availability/impact - Fagbenro and Agboola, 1993; Florence et al., 1992b; Förstner, 1991; Klavins and Cinis, 1992; Krishnamurthy, 1992 (Review of humics and contaminant transport); MacCarthy and Perdue, 1991 (Review of complexation of metal ions by humics); Porta and Ronco, 1993; Tomita, 1993; Wang et al., 1992b; Whiteley and Williams, 1993;

Soil organics after treatment with sewage or waste - Förstner, 1991

I.8 THE EFFECTS OF COPPER ON GROWTH AND DEVELOPMENT

As an essential metal, an adequate supply of copper is necessary for growth and development. When biologically available copper is in excess, however, the metal can be detrimental to growth and development. As a result, the developing organism, and the ageing organism require the correct amount of copper, in a suitable chemical state, to enable normal metabolism. This is true for microorganisms, plants and animals and, incidentally, is true for a range of other trace metals and nutrients.

References dealing with the effects of copper on growth and development are listed under the major group of organisms and, within that heading, under appropriate categories.

Microorganisms

Growth at elevated copper concentrations .... Engel, 1992; Gordon et al., 1993; Malavasic & Cihlar, 1992

Microbial growth near waste sites .... Bolton et al., 1993

Blue-green algae (Cyanobacteria)

Copper inhibition .... Dwivedi et al., 1992

Algae

Growth at elevated levels of copper .... Carpene & Boni, 1990; Wang et al., 1992

Mosses and bryophytes

Growth near mine sites .... Shaw et al., 1991

Forage and domestic grasses and grains

Copper requirements..Agrawal, 1992
Changes in copper requirements during growth.................... Wojcieska et al., 1989
Molybdenum-copper interactions..Nass et al., 1993
Inhibition of germination and growth .... Greipsson, 1992; Hsu & Chou, 1992; Sarada & Polasa, 1992; Singh et al., 1992b
Use of copper for growth control in containerized plants..................Latimer, 1993
Tolerance to elevated metal concentrations............................... Hsu & Chou, 1992
Effects of copper on nitrogen fixation/metabolism......... Lidon & Henriques, 1992a (effects of excess copper); Seliga, 1993 (effects of copper deficiency)
Agricultural practices, soil types and copper effects .... Nemec & Lee, 1992; Serôdio & Novais, 1991
Miscellaneous benefits from copper ....Repka, 1993 (thermoprotection)

Domestic plants

Copper requirements...Hole & Scaife, 1993
Growth response to copper deficiency ....Hole & Scaife, 1993
Copper uptake ....Lisbão et al., 1991
Effect of copper on metabolite production ....Sevón et al., 1992
Effects of excess copper ....Yang & Roru, 1991
Copper in sludge and growth response..Smith, 1992

Native plants

Uptake and accumulation of copper in developing plants........... Novacek, 1983a,b; Svenson & Witte, 1992
Use of copper for growth control in containerized plants....Flanagan & Witte, 1992
Growth and tolerance in metal-rich soils near mines and metal industries................ Jones et al., 1985 (growth inhibition noted); Turner & Dickinson, 1993b; Wozny et al., 1992

Invertebrate animals

Distribution of copper in organisms
Helminth worms (developmental stage)....................Chowdhury & Singh, 1993
Freshwater mussels ....Naimo et al., 1992
Crustaceans...Rao & Govindrajan, 1990
Effect of copper on survival, development or growth
Rotifers ....Snell & Moffat, 1992
Annelid worms...Wiederholm & Milbrink, 1988
Molluscs .... Chang et al., 1993b; D'Aniello et al., 1990; Grapentine, 1992; Soria-Dengg & Ochavillo, 1990
Crustaceans.... de Nicola Giudici & Migliore, 1988; Qi et al., 1991; Wong, 1993
Insects ....Krzysztofiak, 1991; Posthuma et al., 1993; Timmermans et al., 1992; Tranvik et al., 1993
Air/water/sediment quality factors and the effects of copper on growth
Annelid worms.. Ozoh, 1992b
Crustaceans.............................. Yuan et al., 1992 (use of polymeric heavy metal absorbent (PHMA) to remove metal from shrimp rearing systems)
Insects ....Minoranskij & Wojciechowski, 1991

Fish - Effect of copper on survival, development or growth.........Nakagawa & Ishio, 1991

Amphibians - Effect of copper on survival, development or growth................ Mironova & Andronikov, 1992

Domestic animals

Poultry

Tissue metal relationships................................ Szymkiewicz & Niemiec, 1990; Szymkiewicz et al., 1990

Metabolism of copper .... Richards, 1991b

Benefits of copper supplementation.. Li & Wu, 1992

Sheep

Trace element deficiency ....Holmes, 1992; Kolb et al., 1992b

Effects of copper................Grace & Lee, 1988 (on bone mineral content); Kim et al., 1991

Availability and effect of dietary copper.................................Kolb et al., 1992b

Selenium supplementation and the effect of elevated levels of dietary copper ....Angelow & Yanchev, 1991

Cattle

Colostrum as a source of trace metals and minerals for newborn calves... Kume & Tanabe, 1993

Copper in dairy rations..........Graham & Keen, 1992; Jacques & Newman, 1993

Laboratory animals

Rodents

Age-related changes in copper and copper-containing organic agents................ Ceballos-Picot et al., 1992; Martinez Lista et al., 1993; Munim et al., 1992

Exercise, pregnancy and plasma copper levels...................... Lewis et al., 1993b

Changes in metallothionein during pre- and postnatal development................... Chan & Cherian, 1993

Copper content in models of Wilson's disease.......................Kubota et al., 1991

Detrimental effects of copper on development...............Matsumoto et al., 1993

Dogs

Copper deficiency ....Zentek et al., 1991

Humans

Gestation and infancy

Changes in maternal serum copper during pregnancy............Nagra et al., 1991; Yabuki et al., 1991

Maternal and cord blood levels in relation to infant birth weight........................ Wasowicz et al., 1993

Variations in plasma copper levels in preterm infants.............. Burns et al., 1993

Changes in human milk copper levels during lactation ....Anderson, 1993

Elderly

Nutrition and copper requirements .... Ausman & Russell, 1991

Miscellaneous

Periphyton growth.......................Chessman et al., 1992 (no apparent benefit from added trace elements)

I.9 COPPER AND THE INTERACTIONS OF ORGANISMS

Organisms interact in a variety of ways, to the benefit or detriment of each other. The physiological condition of organisms can affect these interactions, a feature that is important when considering essential metals and nutrition or the detrimental effects of excess biological available metal. Anthropogenic stress is the stress produced by the action of humans on ecosystems (Cairns and Pratt, 1990) and can include the effect of anthropogenic metals on aquatic and terrestrial communities.

References cited in this section are those that include copper in discussions of community structure as well as discussions of particular relationships, including parasitism.

Community responses to heavy metals including copper

Freshwater (including laboratory and microcosm studies)............. Clements, 1991; Clements et al., 1992; Dave, 1992; de Nicola Giudici & Migliore, 1988; Glooschenko et al., 1992; Meador et al., 1992; Pratt et al., 1993; Smith & Morris, 1992 (impacts of changing geochemistry on fish assemblages in rivers affected by a gold and copper mine); Sugiura, 1992; van Dijk et al., 1993

Saltwater (including laboratory and microcosm studies).. Prager & MacCall, 1993 (copper was one of a number of metals included as "metal loadings" used for modeling spawning success of three coastal pelagic fish species in southern California); Tkalin et al., 1993; Zhuang & Lin, 1991

Terrestrial (including soil conditions)

Forest communities..Barros Henriques & Hay, 1992; Kopeszki, 1991; Singhal & Soni, 1992

Agricultural lands and domestic plants...................... An et al., 1993b (benefit of mycorrhizal fungi and copper in the growth of apple seedlings); De Cal & Melgarejo, 1992 (interactions of pesticides and mycoflora of peach twigs); Ownley et al., 1992 (soil factors associated with suppression of take-all of wheat by a microorganism); Prasad & Ram, 1992 (benefits of copper and *Rhizobium* innoculation on grain yield of greengram); Smith & Papacek, 1991 (effect of pesticides, among other things, on a predatory mite used to control a pest organism in citrus orchards); Willems et al., 1993b

Industrial and urban soils........................Groudev & Groudeva, 1993 (microbial communities in industrial copper dump leaching operations in Bulgaria); Hashem, 1993; Krzysztofiak, 1991

Heavy metal contaminated soils....................................Roane & Kellogg, 1993

Miscellaneous .... Herd et al., 1993 (metal supplementation effect on virus-challenged steers); Ortel et al., 1993 (effect of metal stress on a host-parasitoid relationship with gypsy moth larvae); Sjögren, 1992

I.10 COPPER, NUTRITION AND FOOD CHAINS

There is continuing interest in the importance of copper as a nutritional requirement and a potential contaminant in food chains. Since copper is one of the trace elements that has been shown to be essential for life, an inadequate supply has been associated with metabolic disturbances (e.g. Warrier et al., 1990), a condition where supplementation can be beneficial (e.g. Specker et al., 1992). Brewer et al. (1993a) point out that the marginal copper intake in American diets, particularly in those of vegetarians, may not be adequate to prevent mild copper deficiency. Turnlund (1989) comments that, for humans, (page 21) "Because Cu absorption and endogenous losses vary with dietary intake, Cu balance can be achieved and status maintained over a relatively broad range of dietary Cu intakes." However, physiological status, age, food nature and metal bioavailability must be considered when contemplating copper requirements (e.g. Lamand, 1991; Lukaski and Johnson, 1992). Copper in food can also affect food quality, becoming involved in the oxidation of lipids (e.g. Yoshida and Niki, 1992).

In environmental situations, a certain level of copper is required for the growth of plants and animals. However, excess copper is of concern because of potential incorporation in component organisms of food webs. A number of references deal with the concentration and chemistry of metals in the environment (e.g. Joanny et al., 1993) and the potential for uptake by organisms (Cooke et al., 1992; Hart and Andrews, 1991; Jones, 1992; Laskowski and Maryanski, 1993; Stewart et al., 1992). (It should be noted that the metals of main concern are mercury, lead and cadmium.) Weis and Weis (1993) examined trophic transfer of copper and arsenic from organisms living near CCA-treated wood. They noted elevated tissue copper levels under both field and laboratory conditions.

Recent food- or nutrient-related references that include information on copper are in a wide range of categories. They are here listed according to the central theme or themes of the reference:

Copper and plants or plant nutrients

- Copper in soils..................... Angelone & Bini, 1992; Baccini & von Steiger, 1993; Bahmaniar et al., 1993; Chen, 1992b; Kim & Thornton, 1993; Kirilynk & Vaculik, 1991; Munkholm et al., 1993
  - Soil testing for available microelements.....................................Watanabe, 1992 (harmful elements/levels)
- Metal content of fertilizers..Charter et al., 1993
- Relationship between copper in soils/sediments and plants (including some references on uptake).....................................Angelone & Bini, 1992; Jackson et al., 1992; Mohapatra et al., 1993; Moreno et al., 1992
- Relationship between copper in soils and domestic plants (includes the use of soil supplements and sewage or sewage sludge) .... Bearce, 1993; Juste & Mench, 1992; Nunez-Moreno & Uvalle-Bueno Inifap-Ciano, 1992; Stiles & Rutzke, 1993; Zafaralla & Mangaban, 1990
- Nutritional requirements of domestic plants ....Misra, 1992
- Metal levels in pasture and fodder plants..................Amirkhanov & Islamov, 1991; Cuesta et al., 1993; Danon & Jakovljevic, 1992; Dragnev et al., 1991 (fodder plants and animal organs as an indicator of pollution); Kidambi et al., 1993
- Relationship between copper in soils and food materials......................... Kirilynk & Vaculik, 1991
- Metal content in plants near industrial areas and minesites..................... Blamowski et al., 1991;Turnau & Kozlowska, 1991

Copper and animals or animal nutrition

- Invertebrates
  - Copper requirements of economically important animals ....Davis et al., 1993
  - Organism copper levels under natural conditions.................Roth, 1992 (reports above average tissue copper concentrations in invertebrates which use hemocyanin as the respiratory pigment)
  - Organism copper levels and anthropogenic metal.........................Alikhan, 1993; Andrzejewska et al., 1990; Cain et al., 1992; Fuge et al., 1993; Gaston & Young, 1992; Kaviraj, 1989; Morgan & Morgan, 1992; Ying et al., 1993
  - Metal transfer in food materials.............................. Amiard-Triquet et al., 1992; Rao & Govindarajan, 1990
  - Effects of metals on feeding .... Wong, 1992
  - Diet and metal levels or effects... Cerda & Olive, 1993; Scott-Fordsmand & Depledge, 1993
- Vertebrates (fish, amphibians, reptiles, birds, mammals)
  - Trophic copper concentrations in fish................................... Emara et al., 1993 (tendency for increased levels of copper at higher trophic levels); Metayer et al., 1992
  - Copper in food materials for fish culture.................Wang, 1991 (contaminants)
  - Copper in birds .... Antoine et al., 1992

Copper in marine mammals .... Antoine et al., 1992
Copper in ungulates (wild) .... Hyvärinen and Nygren, 1993; Niemi et al., 1993
Cheetah nutrition... Dierenfeld, 1993

Domestic animals

General .... Aoyagi & Baker, 1993c (nutritional evaluation of copper-methionine and copper-lysine complexes); Aoyagi et al., 1993a (copper bioavailability); Coleman et al., 1992 (trace metals in edible tissues); Danon & Jakovljevic, 1992 (copper levels in Serbian pasture grounds as a nutritive factor in domestic animals); Dragnev et al., 1991 (fodder plants and animal organs as an indicator of pollution); Migdal et al., 1993

Poultry.. Aoyagi et al., 1993b; Christensen, 1991; Coleman et al., 1992; Kim et al., 1993; Paik et al., 1991; Schöne et al., 1993; van Ryssen & van Malsen (mineral composition of poultry manure with reference feed regulations)

Pigs (copper as a growth promoter) .... Bowland, 1990; Dove, 1993b; Goihl, 1992; Mirando et al., 1993; O'Reilly & Lynch (composition of feed from computerized wet feed system)

Pigs (excess nutritional copper)....... Rambeck et al., 1991; Southern et al., 1993

Sheep, lambs, goats......................... Ali & Al-Noaim, 1992; Grace & Lee, 1988; Hemingway, 1991; Henry et al., 1993b; Krelowska-Kulas, 1992c; Qi et al., 1993; Zelenak et al., 1992

Cattle (copper deficiency) .... Blincoe, 1993a (simulation of bovine copper metabolism); Nakasone et al., 1992

Cattle (copper in food, uptake, deposition, etc.) .... Abdelrahman & Kincaid, 1993; Groot & Gruys, 1993; Iwanska et al., 1992; Kayber et al., 1992; Mansour et al., 1993b; Nockels et al., 1993; Rajora & Pachauri, 1993; Rankin et al., 1993 (nature of broiler litter foodstuff for beef cattle); Rudneva et al., 1992; Son & Son, 1991; Spiekers et al., 1991; Vulink & Drost, 1991

Other .... Ott & Asquith, 1993; Treuthardt, 1992 (mink)

Laboratory animals (including dogs)

General .... Larsen & Sandström, 1992b

Copper deficiency .... Bhathena et al., 1991; Farms et al., 1993; Fields et al., 1993a; Luhrsen et al., 1993; Schelkoph et al., 1993

Dietary copper requirements .... Czarnecki-Maulden et al., 1993

Dietary materials (other than sugars) and copper.. Gonzalez-Reimers et al., 1993; MacDonald et al., 1991; Shah et al., 1991; Van den Berg & Beynen, 1991, 1992

Copper and dietary sugars......... Kashimura et al., 1992; Kohls & Doulas, 1993; Lewis et al., 1993a (fructose and low copper diets); Lure et al., 1993; MacDonald et al., 1991; Rader et al., 1991; Rizkalla et al., 1993 (copper and fructose can interact to affect insulin levels and binding); Van den Berg et al., 1993b; Wapnir & Davas, 1992, 1993; Werman & Bhathens, 1992, 1993a,b

Responses to different intakes and modes of trace metal supplementation.......... Klevay & Saari, 1993; Larsen & Eggum, 1991; Markovits et al., 1992; Matsuda et al., 1990, 1992

Miscellaneous .... Klevay, 1993

Human nutrition

Dietary metals and tissue metal concentrations....................... Sandford & Kissling, 1993

Growth/condition and nutrient status

Infants..Bradley et al., 1993; Katz et al., 1992; Richmond et al., 1993

Children........................Ahmed et al., 1993; Sui et al., 1991b; Zieba et al., 1992

University students..Barbera et al., 1993

Adults...Milne & Nielsen, 1992

Older adults and elderly.................Ausman & Russell, 1991; Goren et al., 1993; Hermann et al., 1992, 1993a; Kerstetter et al., 1993; Umoren, 1989

Copper and weight loss...Lykken & Klevay, 1992

Various populations ....Benemariya et al., 1993a; Klevay et al., 1992; Milman et al., 1993; Moreiras et al., 1993; Shatenstein et al., 1993

Nutrient abnormalities and physiological status......................Beach et al., 1992; Bogden et al., 1993; McClung et al., 1993; Yasufuku et al., 1991

Dietary trace metals and physical activity.................................... Anderson, 1992a

Supplementation

Elements in supplements ....Hight et al., 1993

Dietary mineral supplements and health......................................Allegrini, 1992

Supplementation by athletes...Bazzarre et al., 1993

Supplementation in parenteral nutrition...................Frankel, 1993; Okada, 1991

Copper in food (includes food web/chain transfer)

Miscellaneous Arcos et al., 1993; Chang & Sibley, 1993 (note that the crustacean *Daphnia magna* may have a regulatory mechanism for copper); Chevalier & Rupp, 1993; Cimino & Ziino, 1983b; Cimino et al., 1992; Compère et al., 1993; Dabeka & McKenzie, 1992; Dikanovic-Lucan et al., 1992; Emara et al., 1993; Falandysz & Kotecka, 1991b; Ianov et al., 1992; Ivanov et al., 1990, 1992; Karahadian & Lindsay, 1989; Kohiyama et al., 1992c,d; Mochizuki et al., 1990; Moreiras et al., 1992; Ramanathan & Das, 1993; Refsgaard et al., 1992 Weis & Weis, 1993; Wucherpfinnig, 1992a,b; Yasui, 1992; Yoshida & Senda, 1993; Zhang et al., 1991c

Milk ....Garg et al., 1993; Hurley & Lönnerdal, 1988; López Mahia et al., 1991

Grain and cereal products`..............Gahlawat & Sehgal, 1993; Grüner et al., 1992; Krelowska-Kulas, 1992b; Tanusi et al., 1992; Tiscornia et al., 1991; Vaquero et al., 1992; Villareal et al., 1991; Wenk et al., 1992

Soybean.. Yukawa & Kitao, 1992; Zhang et al., 1991c

Vegetables and fruits .... Kot & Bulinski, 1988; Peron et al., 1991; Schuhmacher et al., 1993a

Meat.. Golow, 1993

Tea and coffee...............................Falandysz & Kotecka, 1991a; Zhao et al., 1990

Wines and spirits.. Andrey et al., 1992; Enkelmann, 1992; Ewaidah, 1993; Faria & Pourchet, 1987; Faria et al., 1993; Kern et al., 1992a; Redl, 1992

Tobacco and tobacco products .... Maier et al., 1993

Herbs, herbal plants and traditional Chinese drugs...................Wong et al., 1993b; Wu, 1992b

Copper levels and the nature of food materials........... Chikkasubbanna et al., 1990; Cotterill et al., 1992; Ozkaya & Kahveci, 1989; Rincón et al., 1993; Simko et al., 1992

Estimation and information on nutrient metal bioavailability.................................. Barbera et al., 1991; Beuggert et al., 1993; Brzozowska et al., 1991; Johnson et al., 1992a; Randhawa & Kawatra, 1993; Wolf, 1991; Wolters et al., 1992, 1993

Copper in water: Water is included in this section because it is considered an ingestible "nutrient". Copper is found naturally in water but it can also come from copper-containing tubing or piping used for dispensing drinking water or hot water. In a workshop on plumbing materials and drinking water quality (Sorg and Bell, 1986), it is pointed out that copper has a number of good features (including quality manufacturing and the industrial use of technology for removing the drawing chemicals) but that corrosion can occur with the introduction of metal into the water. This section includes references that deal with the beneficial and detrimental effects of copper in drinking water or domestic hot water.

General information on heavy metals in drinking water (including bibliographies)... U.S. National Technical Information Service, 1993d,e

Guidelines for Drinking-Water Quality.........................Mehta & Dass, 1992 (water storage practices); Ramaley, 1993 (monitoring and control for compliance with the U.S. Environmental Protection Agency's lead and copper rule); Schock & Lytle, 1993 (Corrosion control principles and strategies for reducing lead and copper in drinking water systems); Sorg & Bell, 1986 (Plumbing materials and drinking water quality); Symons, 1986 (Summation of findings in the workshop on "Plumbing materials and drinking water quality"); World Health Organization, 1993a

Intake of copper through drinking water .... Alena et al., 1991

Copper as a controlling agent for Legionnaires' disease............ Colville et al., 1993

Resistance of bacteria and fungi to copper in humidifiers............ Kay & Ford, 1993

Copper as a catalyst in reducing nitrate levels in drinking water...... Sell et al., 1992

Copper alloys for desalination plants..................................... Shams El Din, 1993a (copper nickel alloys were developed to withstand high water velocities. "All copper base alloys are prone to failure in polluted seawater containing sulphides and ammonia.")

Corrosion in domestic drinking water installations............................ Gómez Bárez et al., 1991a, b (different water treatments on heavy metals concentrations in drinking water); Wagner, 1992 (points out that major problems of copper uptake from the water are found mainly in waters of low and very low pH); Wysock et al., 1993 (statistical procedures for corrosion studies)

Copper in wells or ground water.............................. Assmuth & Strandberg, 1993; Hegde & Puranik, 1992; Ipinmoroti, 1993

Copper in utensils...Kataeva, 1991 (metal leaching from polymeric materials); Mehta & Dass, 1992; Saito et al., 1991; Tomita et al., 1992

Effects of copper in drinking water..Bhave et al., 1992 (report the possibility that Indian childhood cirrhosis (ICC) is due to the "synergistic toxicity of copper and a plant biocide, such as pyrrolizidine alkaloid."); Gaida & Radtke, 1990b (in German - discussion of a Bavarian family that reportedly was exposed to poisoning from copper in well water; data are provided on the effect of copper-containing water on the growth of 33 "cress seeds"); Sethi et al., 1993 (a discussion of the role of copper in Indian childhood cirrhosis (ICC); the authors point out that dietary copper as a source of ICC seems unlikely. They suggest that the most probable cause is a defect in the metabolism of copper in ICC patients.)

Miscellaneous......................... Allen & Klevay, 1994 (copper as an antioxidant nutrient for cardiovascular health); Olasupo et al., 1993 (copper tolerance); Pilková et al., 1990 (browning reactions of Heyns rearrangement products)

I.11 ORGANISMS AS INDICATORS OF COPPER DEFICIENCY AND EXCESS

With copper and organisms, when the term "deficiency" or "excess" is used it is intended to imply physiologically abnormal conditions of metal bioavailability. As a result, organisms can serve as indicators of copper deficiency or excess and, when properly used, indicators of metal bioavailability.

The biological impacts of industry are often associated with the release of anthropogenic metals (e.g. Berndtsson, 1993; Salomons, 1988). As a result, monitoring programs often include biological assays of metal impact and, hopefully, metal bioavailability (e.g. Isom, 1992a; Landis et al., 1993; Mayes and Barron, 1991; Peakall and Shugart, 1993; Phillips and Rainbow, 1993; United Nations Environment Programme, 1990). Biological indicators, or monitors, have included both communities (e.g. Clements, 1991) and species (see, for example, the reviews of algal toxicity testing by Thursby et al., 1993 and marine mollusc toxicity testing by Hunt and Anderson, 1993). Changes in both communities and species are also used as indicators of environmental change occurring as a result of man (e.g. Cairns and Pratt, 1990) or the results of reclamation efforts (e.g. Fucik et al., 1991). However, the proper use of organisms as indicators requires an understanding both of the biology of the organism and the relationship it has with metals, including metal requirements, uptake and metabolism (e.g. Mackun et al., 1993).

Recent references that deal with the use of organisms, or environmental media, as indicators of copper (or general metal) deficiency and excess include:

General - monitoring programmes

Examples..Halbrook et al., 1991
Capabilities...Fryer & Nicholson, 1993
Peat as a medium for historical monitoring...............................Jones & Hao, 1993

Environmental media

Seawater ....Hardy & Cleary, 1992
Suspended matter ....Hong et al., 1992; Ingri et al., 1993
Sediments........... Alden & Rule, 1992; Burgess et al., 1993b,d; Chen et al., 1992g; de Vevey et al., 1993; Phelps, 1993; PTI, 1991 (reference area performance standards for Puget Sound sediments); Reichardt et al., 1993; Tay et al., 1992; Ying et al., 1992; Zhang et al., 1992a
Industrial effluents ....Costan et al., 1993
Mine tailings.. Schroeter & Sand, 1993; Zhan et al., 1992
Wastewater ....Bitton et al., 1992b

Groups of organisms

Metal concentrations in groups of organisms.......................................Roth, 1992
Communities as indicators of metal impact.........Clements et al., 1992 (includes the evaluation of an index of community sensitivity); Gee et al., 1992
Species diversity as an indication of metal impact.......................... Kopeszki, 1991
Phytoplankton as indicators .... Lapota et al., 1993
Animal biomarkers as pollution indicators...Peakall, 1992
Crustaceans as indicators... Engel & Brouwer, 1993
Insects as indicators... Krzysztofiak, 1990

Techniques

Establishing a bioassay system .... Emans et al., 1993; Sjögren, 1992
Microcosm use ....Pratt et al., 1993; Rozycki, 1993; Sugiura, 1992
The use of marine experimental enclosures............................... Chen et al., 1992g; Isom, 1992b; Li et al., 1992a,b; Wong et al., 1992; Wu et al., 1992b; Xu et al., 1992a; Zhang et al., 1992a
Soil test systems ....Chander & Brookes, 1991b; Obbard & Jones, 1993b; Vangronsveld & Clijsters, 1992
Biological nitrogen fixation...Mårtensson, 1993
Physiological tests ....Laakso & Michelsson, 1992; Ohno et al., 1992b; Pérez-García et al., 1993

Biochemical detection systems............................Bragadin et al., 1992; Chander & Brookes, 1991b; Jimenez & Stegeman, 1990; Johnson et al., 1993c; Laihia et al., 1993; Mason & Storms, 1993; Ogawa et al., 1992; Percival, 1993; Petkau et al., 1989; Zürn & Müller, 1993

Metallothionein..................Engel & Brouwer, 1993; Lindahl & Moksnes, 1993; Micallef et al., 1992; Raspor & Pavicic, 1992

Cytotoxicity tests..Babich & Borenfreund, 1993

Genetic effects of excess metal...Hummel et al., 1991

Variation in metal sensitivity............................Chappell, 1992 (not specific for any metal); Volkov et al., 1992; Tubbing et al., 1993b

Analysis of bioassay material..Alimonti et al., 1989; Steinnes et al., 1993; Viñas et al., 1993

Metal speciation.................................Florence et al., 1992a; Schwedt et al., 1993; Ying et al., 1992

Water and sediment genotoxicity measurements....................Langevin et al., 1992 (important work although note that copper is not one of the metals measured)

Monitoring domestic animals..Keirs et al., 1991

Variability of treatments/results.............Alden & Rule, 1992; Ankley et al., 1993b; Nolan, 1991; Nyholm et al., 1992; Schaug et al., 1990

Reference materials for bioassay purposes or trace metal analysis of bioassay materials

Establishing reference materials..Markert, 1992

Botanical reference materials ....Kucera & Soukal, 1993b; Kucera et al., 1993; Ward et al., 1992

Domestic vegetables and plants........Kucera et al., 1993; Novozamsky et al., 1993; Ward et al., 1992; Zeisler et al., 1993

Human food materials.. Kucera & Soukal, 1993b; Tahvonen & Kumpulainen, 1992

Trace element analysis of plankton used to monitor uptake by food chain/web organisms ....Quevauviller et al., 1993

Invertebrate animals..Jaffe et al., 1992

Economically important fish...Quevauviller et al., 1992

Domestic animals and animal parts...An et al., 1993a

Human reference materials.. Okamoto, 1992

Microorganisms

Microbial bioassay tests....................Balsalobre et al., 1993; Campbell et al., 1993; Codina et al., 1993; Hardoyo et al., 1993; Mazidji et al., 1992; Rozycki, 1993; Searle et al., 1992; Torslov, 1993; Wei & Morrison, 1992

The use of bacterial bioluminescence as an indicator of copper bioavailability......... Gangolli et al., 1993; Ramaiah & Chandramohan, 1993; Thomulka et al., 1993

Determination of soil bacterial types .... Rodriguez et al., 1993

Evaluation of bacterial growth and leaching activity with copper-bearing minerals.. Bustos et al., 1993

Cyanobacteria (blue green algae) as indicator organisms for anthropogenic copper ....Lee et al., 1993d

Plants

Algae

Metal levels in indicator organisms................................... Barreiro et al., 1993; Rajendran et al., 1993; Stewart et al., 1992; Wang et al., 1990

Periphyton as indicators ....Ramelow et al., 1992b

Phytoplankton and primary productivity in phytoplankton in enclosures............ Qian et al., 1992

Growth and physiological work with indicator organisms............ Pandard et al., 1993; Rachlin & Grosso, 1993

Assessment of herbicide phytotoxicity.............................St-Laurent et al., 1992

Lichens

Metal levels in indicator organisms...................................... Blyum et al., 1988; Kryuchkov & Syroid, 1990; Lawrey, 1993; Sloof & Wolterbeek, 1993a

Source of metal in organism...................................Sloof & Wolterbeek, 1993b

Metal tolerance ....Garty, 1992

Bryophytes

Metal levels in indicator organisms...........................Józwik, 1990, 1991, 1992; Józwik et al., 1991, Józwik & Magierski, 1992, 1993; Schmid-Grob et al., 1992;

Use of bryophytes as indicators...Mersch et al., 1993

Fungi

Metal uptake and levels in indicator organisms....................Borella et al., 1991; Novácek et al., 1990; Quinche, 1993

Use of fungi as indicators............Koch et al., 1993; Kungolos & Aoyama, 1992

Gymnosperms and Angiosperms

Metal uptake and levels in indicator organisms.................. Baucells et al., 1989; Jenner & Janssen-Mommen, 1993; Józwik, 1990, 1991; Józwik & Mzgierski, 1992, 1993; Józwik et al., 1991; Novácek & Matovic, 1992; Stewart et al., 1992; Zayed et al., 1992

Metal tolerance and toxicity .... Farago & Mehra, 1992; Vidakovic et al., 1993

Biogeochemical surveys ....Pandolfini & Pancaro, 1993

Estimation of copper nutrient status in plants ....Onyezili & Harris, 1993; Rao & Ownby, 1993; Ruszkowska et al., 1990, 1991

Fodder plant tissue metal concentration as an indication of metal availability to domestic animals.. Dragnev et al., 1991

Animals

Invertebrates

Metal levels in indicator organisms........................... Cheung & Wong, 1992a,b; Hameed & Raj, 1990; Harms & Huschenbeth, 1991; Marmolejo-Rivas & Paez-Osuna, 1990; McEvoy & Sundberg, 1993; Naimo et al., 1992; Paez-Osuna et al., 1993; Perdicaro, 1989; Stewart et al., 1992; Van der Velde et al., 1992; Verdenal et al., 1990; Zauke et al., 1992

Protozoans... Forge et al., 1992

Sponges .... Richelle-Maurer et al., 1991; Verdenal et al., 1990

Nematode worms.......Donkin & Dusenbery, 1993; Stringham & Candido, 1993

Rotifers...Snell & Moffat, 1992

Annelid worms................................. Ozoh, 1992a,b,c; Wiederholm et al., 1988

Molluscs other than mussels and oysters........................Baudo & Galanti, 1988; Berger & Dallinger, 1993; Fuge et al., 1993; Greig & Pereira, 1993; Harrel & McConnell, 1992; Huebner & Pynnönen, 1992; Institute Francais de Recherche pour L'Exploitation de la Mer, 1991 (note trend of increasing copper levels in mussels and oysters which they attribute to the use of copper-based antifouling paints following TBT ban); Paez-Osuna et al., 1993; Simkiss & Watkins, 1991; Zaroogian et al., 1992

Mussels... Eertman et al., 1993; Fuge et al., 1993; Huebner & Pynnönen, 1992; Hameed & Raj, 1990; Jacobson et al., 1993; Majori et al., 1991a,b; Marmolejo-Rivas & Paez-Osuna, 1990; Mersch & Pihan, 1993; Mersch et al., 1992; Naimo et al., 1992; Pavicic et al., 1993; Reincke, 1992; Robinson et al., 1993; Van der Velde et al., 1992;

Oysters ....Ikuta, 1991a,c; Ikuta & Morikawa, 1991; Institute Francais de Recherche pour L'Exploitation de la Mer, 1991; Perdicaro, 1989

Crustaceans other than barnacles.............Alikhan, 1993; Borgmann et al., 1993; Brandt et al., 1993; Brouwer et al., 1993; Canli & Furness, 1993a; Centeno et al., 1993; Gautam, 1990; Greig & Pereira, 1993; McGee et al., 1993; Qi et al., 1991; Rainbow et al., 1993; Schlenk et al., 1993; Steele et al., 1992; Van Hattum et al., 1993; Winger et al., 1993

Barnacles ....Zauke et al., 1992

Insects ....Cain et al., 1992; Nelson & Roline, 1993; Whipple & Dunson, 1993

Echinoderms .... Bay et al., 1993

Vertebrates

Metal levels in indicator organisms.................................... Hylland et al., 1992; Kowalewska & Korzeniewski, 1991; Malyarevskaya & Karasina, 1991

Fish ....Burgess et al., 1993a; Eggens et al., 1992; Hernandez et al., 1992; Hylland et al., 1992; Khan & Weis, 1993; Kowalewska & Korzeniewski, 1991; Lin & Dunson, 1993; Nakagawa & Ishio, 1991; Stagg et al., 1992; Thomas & Smith, 1993

Amphibians..Naitoh & Wassersug, 1992

Birds.. Antoine et al., 1992; Brennan et al., 1992; Shibata et al., 1992a

Marine mammals................................. Antoine et al., 1992; Frank et al., 1992a

Native terrestrial mammals.. Launer et al., 1991

Domestic animals

Fowl ....Szymkiewicz & Niemiec, 1990; Szymkiewicz et al., 1990

Sheep (including wool)..........................Bires et al., 1991b; Lee & Grace, 1988

Cattle.......................................Mulryan & Mason, 1992; Rudneva et al., 1992;

Laboratory models of human diseases.................................... Schilsky et al., 1993

Human tissues and hair

Hair metal concentration as an indicator.............................Donma et al., 1992; Watanabe et al., 1992; Yoshinaga et al., 1993

Serum trace metal concentration as an indicator..................... Jiang et al., 1991; Ma & Jiang, 1993

Tissue copper concentrations in abnormal tissues..............Yoshida et al., 1992a

Metallothionein expression of abnormal growth.................... Zelger et al., 1993

Miscellaneous ....Fazzin et al., 1987; Houwen et al., 1993; Johnson & Dufault, 1993b; Mizutani et al., 1990a; Sergeant & Johnson, 1993; Turnlund, 1991

I.12 TOXICITY

"The noun 'toxicity' is defined as the quality, relative degree, or specific degree of being toxic or poisonous. As such, it is a term often used in documents discussing detrimental as well as beneficial effects of copper. Unfortunately, there is often the misunderstanding that copper is detrimentral until proven beneficial (i.e., guilty until proven innocent). Copper is an essential metal, required for life; too much copper can be detrimental if it is in a biologically available chemical form" (1992 I.C.A. review). However, the biological impact of any excess available copper is dependent on a number of environmental factors with which organisms interact (e.g. Ozoh, 1992b).

The ability of excess biologically available copper to limit biological activity makes it very useful in controlling certain types of undesirable growth. Copper complexes have, for example, been demonstrated to have cytotoxic, antitumour, anticarcinogenic and antimutagenic activity (e.g.Arena et al., 1993). Arena et al (1993), however, point out (abstract) "... that the cytotoxic activity is related to the amount of copper(II) contained in the tested compounds". Copper is also useful as an algicide and in the treatment of parasites (e.g. Straus, 1993).

Even though copper is a required trace metal, its presence in excess can have unwanted detrimental effects under certain conditions. As a result, it is one of the metals frequently considered in the assessment of environmental risk (e.g. Tölgyessy, 1993). Review papers have appeared in the recent literature (e.g. Glime, 1992) as well as a number of papers in symposia on aquatic toxicology and risk assessment (e.g. Landis et al., 1993; Mayes and Barron, 1991) or been reviewed in documents such as Reish et al. (1992). Cox (1991) provides a review of the use and toxicity of chromated copper arsenate (CCA) and Talakin et al. (1991a,c) provide discussions on the toxicity of copper chloride (in Russian) while several papers discuss the biological impacts of anthropogenic copper as either primary or secondary agents in particular areas or with particular groups of organisms (e.g. Abdel-Hamid et al., 1993; Antoine et al., 1992; Cornwell and Stevenson, 1990; Finlayson et al., 1993; Gadd, 1993; Guzmán and Jiménez, 1992; Hardy and Cleary, 1992; Jones et al., 1985; Kessler, 1991; Lavie and Nevo, 1991; Mcllveen, 1993; Prager and MacCall, 1993). A number of these deal with aquatic sediments which contain a wide range of materials, including copper (Burgess et al., 1993c,d; Dave, 1992; Gee et al., 1992; Hoke et al., 1993; Johnson et al., 1992b; Phelps, 1993; Santiago et al., 1993; Tay et al., 1992; Yi et al., 1992). The biological effects of excess anthropogenic metal can range from intracellular responses (e.g. Brown, 1993) to community responses (e.g. Clements, 1991; Mårtensson, 1992; Miller et al., 1992). Copper toxicity has been reported in domestic animals (e.g. Vinlove et al., 1992), often a result of particular problems related to the food available to the animal. Certain organisms are also able to tolerate exceptionally high levels of copper and may even be used to extract metals from mine wastes or other environments containing excess natural or anthropogenic metal (e.g. Burgstaller and Schinner, 1993; Gadd, 1992). Recent references are grouped by topic or organism type:

Monitoring - role, tests and analysis

Reviews........Fucik et al., 1991 (the role of biomonitoring in measuring the success of reclamation at a hazardous waste site); Hunt & Anederson, 1993 (toxicity testing with marine molluscs); Isom, 1992a (literature review of biomonitoring); Thursby et al., 1993 (review of current status of marine algal toxicity testing in the United States)

Analytical techniques and their evaluation..............Allen et al., 1993; Ankley et al., 1993a,b; Babich & Borenfreund, 1993; Bitton et al., 1992a,b; Bragadin et al., 1992; Codina et al., 1993; Collins et al., 1991; Jenner & Janssen-Mommen, 1993; Kwan, 1993; Mazidji et al., 1992; Obbard & Jones, 1993b; Reichardt et al., 1993; Rozycki, 1993; Schubauer-Berigan et al., 1993; Strotmann et al., 1992; Sugiura, 1992; Thomulka et al., 1993; Vangronsveld & Clijsters, 1992

Regional applications..Hall et al., 1992

Statistical tests and evaluations............Clarke & Ainsworth, 1993; Clements et al., 1992; Costan et al., 1993; Emans et al., 1993; Host et al., 1991; Nicolaidou et al., 1993 (use of multivariate techniqes to compare two different types of pollution - copper is not discussed as a separate entity); Nyholm et al., 1992; Ryan et al., 1992;

Sensitivity and tolerance to copper - differences in sensitivity can exist not only between different kinds of organisms but also within a single species of organism as a result of growth or physiological stress. Apparent differences in sensitivity may also be due to differences in the biological availability of copper, a result of environmental conditions and metal speciation.

Sensitivity................... Centeno et al., 1993; Cerda & Olive, 1993; Chappell, 1992; Lewis & Horning, 1991 (although this publication uses cadmium, the concept that tests results can vary with temperature are important in toxicity work with any metal); Tubbing et al., 1993b; West et al., 1993a

Tolerance/resistance .... Abraham et al., 1992; Boyd & Martens, 1992 (This is an excellent reference dealing with possible reasons for metal hyperaccumulation by plants. The authors identify tolerance, drought resistance, interference, inadvertent uptake and defence against herbivores as possible mechanisms for hyperaccumulation.); Bradley et al., 1992 (a general paper on a molecular mechanism of adaptation in an estuarine copepod crustacean; without direct reference to copper); Cooksey, 1993; Cumming & Tomsett, 1992); Farago & Mehra, 1993; Fitch et al., 1993; Fuentealba et al., 1993; Han et al., 1993; Kay & Ford, 1993 (resistance of bacteria and fungi to copper and silver ions used in disinfection of ultrasonic and residential humidifiers); Meharg, 1993; Michaelis & Rieger, 1992; Sanglimsuwan et al., 1993; Silver, 1993; Sundin & Bender, 1993; Tandeau de Marsac & Houmard, 1993; Twiss et al., 1993; Volkov et al., 1992 (in a discussion of regional characteristics of resistance of hydrobionts to metal toxicity, the authors state that "The application of a uniform system of toxicological regulations that ignores regional variations is biologically unsound"); Yang & Cooksey, 1992; Yazgan et al., 1993

Environmental and laboratory factors affecting apparent sensitivity/tolerance......... Alden & Rule, 1992; Bagy et al., 1991; Borgmann et al., 1993; Florence et al., 1992a,b; Gowrinathan & Rao, 1992; Gu et al., 1991b; Isayeva & Kozinenko, 1992; Jop et al., 1991; Meador et al., 1993; Mullick & Konar, 1991; Rhee & Thompson, 1992; Wataha et al., 1993; Wu et al., 1992c; Yarzhombek et al., 1991

Miscellaneous................................ Giroussi et al., 1993 (technique for determining tetrathiomolybdates, an antidote to copperintoxication);

References on toxicity and tolerance/resistance in various types of organisms

Reviews and literature lists................................. Folmar, 1993; National Technical Information Service (U.S.), 1993h

Bacteria and yeasts ...... Amoroso et al., 1993; Bååth, 1992; Balsalobre et al., 1993; Birsch et al., 1993; Chao & Chen, 1991; Chen et al., 1993d; Collett, 1992; Giller et al., 1993; Gordon et al., 1993a; Harwood & Gordon, 1993; Hiroki, 1992; Hsu & Hsu, 1991; Jannasch et al., 1992; Kaur et al., 1993; Koch et al., 1993; Lee et al., 1992a; Lim & Cooksey, 1992, 1993; Malavasic & Cihlar, 1992; Mills & Cooksey, 1992; Mills et al., 1993; Olasupo et al., 1993; Pohronezny et al., 1992; Roane & Kellogg, 1993; Rogers, 1991 (Ph.D. thesis); Rowbury & Hussain, 1992; Silva & Hofer, 1993; Springael et al., 1993; Sundin et al., 1993; Tomsett, 1993; Tørsløv, 1993; Voloudakis & Cooksey, 1992; Voloudakis et al., 1993; Whiteside, 1991 (Ph.D. thesis); Williams et al., 1993; Wu, 1992a; Zhou & Thiele, 1993

Algae..................Augier et al., 1992b; Carpenè et al., 1992; Gensemer et al., 1993; Pandard et al., 1993; Pellegrini et al., 1993; Rao & Gowrinathan, 1992; St-Laurent et al., 1992; Wang et al., 1992b

Plants .... Gimenez et al., 1992; Hsu & Chou, 1992; Jackson & Lee, 1993; Lin, 1991b (Ph.D. thesis); Rhoads et al., 1992; Salt, 1989 (Ph.D. thesis); Schat et al., 1993; Schumacher et al., 1993; Searcy & Macnair, 1993; Turner & Dickinson, 1993a

Plant toxicity on sewage sludge treated agricultural land........... Chang et al., 1992; Chaudri et al., 1993b

Invertebrates (including protists)

- Protozoans..Forge et al., 1992; Janssen et al., 1992; Kramhoft & Jessen, 1992; Sekkat et al., 1992
- Coelenterates ....Hawker & Connell, 1992
- Rotifers.. Ferrando et al., 1993; Porta & Ronco, 1993; Snell & Moffat, 1992
- Nematode worms.. Donkin & Dusenbery, 1993
- Annelid worms................................. Ozoh, 1992a,b,c; Wiederholm et al., 1988
- Molluscs ....Abou-El-Hassan et al., 1990; Al-Sabri et al., 1993; Hole et al., 1993; Huebner & Pynnönen, 1992; Jacobson et al., 1993; Kraak et al., 1993; Kumar et al., 1992; Lagerspetz et al., 1993; Raspor & Pavicic, 1992; Ringwood & Brouwer, 1992; Soria-Dengg & Ochavillo, 1990
- Crustaceans.......................Brandt et al., 1993; Daly et al., 1992; Gautam, 1990; Jop et al., 1993; Koivisto et al., 1992; Lindahl & Moksnes, 1993; Maund et al., 1992; Nonnotte et al., 1993; Reish, 1993; Vijayaraman & Geraldine, 1992; Wong, 1992; Wong et al., 1993a
- Insects .... Bozsik, 1991a,b; Gintenreiter et al., 1993b

Vertebrates (excluding humans)

- Fish .... Cicik & Erdem, 1992; Folmar, 1993; Heath, 1991; Hickie et al., 1993; Jop et al., 1993; Laurén, 1991; Lin & Dunson, 1993; Marek et al., 1991; Mullick & Konar, 1992; Nakagawa & Ishio, 1991; Saksena & Pandey, 1991; Wilson & Taylor, 1993a,b
- Amphibians... Luo et al., 1993c
- Birds.. Kobayashi et al., 1992
- Domestic animals...................................Bires et al., 1991b; Botha et al., 1992; Wang et al., 1992f
- Laboratory animals (and cells)....................................... Nakayama et al., 1992; Neizvestnova et al., 1992; Ogawa et al., 1992; O'Rourke, 1991 (Ph.D. thesis); Reeves & Nelson, 1991; Toussaint & Nederbragt, 1993

Humans (and cells) .... Agarwal et al., 1993; Steffensen et al., 1992

Table 1. Selected toxicity values. (See original publication for details of tests, including the chemical nature of the copper that was used.) "Nature" = nature of test (e.g. 96-h LC50), left blank if not provided in original reference. EC50 = effective concentration causing 50% reduction in some functional process like feeding; IC50 = concentration causing 50% inhibition; LC50 = concentration causing 50% mortality; LT50 = time to 50% mortality at a particular concentration of toxicant; TLm = median tolerance limit.

Name	Nature	Level	Reference
BACTERIA & FUNGI			
Saccharomyces cerevisiae			
IC50 growth	Cupric chloride	162 mg/L	Koch et al., 1993
	Cupric nitrate	193 mg/L	"
	Cupric sulfate	271 mg/L	"
Pseudomonas fluorescens			
16-hEC50 growth	Cu^{2+}	12.7 mg/L	Tørsløv, 1993
ALGAE			
Selenastrum capricornutum			
96-h EC50 growth	Cu^{2+}(microplate)	65.7 mg/L	St-Laurent et al., 1992
INVERTEBRATES			
Protozoans			
Colpoda cucullus			
EC50 death	Cu^{2+}	0.015 mmol/L	Janssen et al., 1992
Rotifers			
Brachionus calyciflorus			
5-hEC50 feeding	"Cu"	0.034 mg/L	Ferrando et al., 1993
Annelid worms			
Hediste diversicolor			
96-h LC50	"copper" at various salinities (S) & temperatures (T)		
	S(7.6), T(22)	339 mg/L	Ozoh, 1992c(also see 1992b)
	S(22.8), T(12)	900 mg/L	"
Molluscs			
Anodonta cygnea glochidia			
48-h EC50	"Cu"	5.3 mg/L	Huebner & Pynnönen, 1992
Anodonta grandis			
24-h EC50	"Cu"	33 mg/L	Jacobson et al., 1993
Biomphalaria alexandrina			
24-h LC50	Copper Sulfate	0.66 ppm	Abou-El-Hassan et al., 1990
Biomphalaria glabra			
24-h LC50	{Cu}(pH8)	0.79 mg dm^{-3}	Al-Sabri et al., 1993
24-h LC50	(+ kaolinite)	0.47 mg dm^{-3}	"
24-h LC50	(+ bentonite)	0.83 mg dm^{-3}	"
Bulinus truncatus			
24-h LC50	Copper Sulfate	0.36 ppm	Abou-El-Hassan et al., 1990

Tridacna derasa (one-hour old embryos)
    50% mortality "Cu"0.1 mg/L (added copper) .... Soria-Dengg & Ochavillo, 1990
Villosa iris
    24-h EC50 "Cu"........................27 mg/L .... Jacobson et al., 1993

Crustaceans
Bosmina longirostris
    48-h EC50 fed "Cu"........................3.7 mg/L .... Koivisto et al., 1992
    48-h EC50 unfed "Cu"........................1.4 mg/L .... Koivisto et al., 1992
Ceriodaphnia quadrangula
    48-h EC50 "Cu"....................0.041 mg/L .... Qi et al., 1991
Chydorus sphaericus
    48-h EC50 fed "Cu"........................7.6 mg/L .... Koivisto et al., 1992
    48-h EC50 unfed "Cu"........................3.3 mg/L .... Koivisto et al., 1992
Daphnia carinata
    48-h EC50 "Cu"....................0.052 mg/L .... Qi et al., 1991
Daphnia galeata
    48-h EC50 fed "Cu"........................7.4 mg/L .... Koivisto et al., 1992
    48-h EC50 unfed "Cu"........................4.1 mg/L .... Koivisto et al., 1992
Daphnia magna
    48-h EC50 fed "Cu"......................49.5 mg/L .... Koivisto et al., 1992
    48-h EC50 unfed "Cu"......................11.3 mg/L .... Koivisto et al., 1992
    48-h EC50 "Cu"....................0.053 mg/L .... Qi et al., 1991
Daphnia pulex
    96-h LC50 "Cu"...........................3 mg/L .... Jop et al., 1993
    48-h EC50 fed "Cu"......................12.2 mg/L .... Koivisto et al., 1992
    48-h EC50 unfed "Cu"........................3.4 mg/L .... Koivisto et al., 1992
Diaphanosoma brachyurum
    96-h LC50 "Cu"....................0.004 mg/L .... Gautam, 1990
Eucyclops speratus
    96-h LC50 "Cu"......................0.15 mg/L .... Gautam, 1990
Gammarus pulex
    Lowest observed effective concentration (LOEC)
    100 day "Cu"......................14.6 mg/L .... Maund et al., 1992
Machrobrachium rude
    96-h LC50 "Cu"....................0.018 mg/L .... Vijayaraman & Geraldine, 1992
Metapenaeus ensis "Cu"
    48-h LC50 - Protozoeal stage III.......0.16 mg/L .... Wong et al., 1993a
    48-h LC50 - Mysid stage III.............1.58 mg/L .... "
    48-h LC50 - Postlarva.......................4.76 mg/L .... "
Moina macropa
    48-h LC50 "Cu"......................0.08 mg/L .... Wong, 1992
Neomysis mercedis
    96-h LC50 copper sulfate.........150 mg/L .... Brandt et al., 1993

FISH

Fathead minnow (*Pimephales promelas*)
    96-h LC50 "Cu".......................180 mg/L .... Jop et al., 1993
Rainbow trout (*Oncorhynchus mykiss*)
    144-h LC50 - Alevin"Cu"...............18, 19 mg/L .... Hickie et al., 1993

Fundulus heteroclitus			
96-h LC50	"Cu"	1.7 mg/L	Lin & Dunson, 1993
Oryzias latipes			
48-h LC50 - egg	Cu^{2+}	>3.00 mg/L	Nakagawa & Ishio, 1991
48-h LC50 Larva	Cu^{2+}	0.55 mg/L	"
48-h LC50 Adult	Cu^{2+}	1.58 mg/L	"
Rivulus marmoratus			
96-h LC50	"Cu"	1.4 mg/L	Lin & Dunson, 1993

II - COPPER AND MAN

II.1 USES OF COPPER

Man has made use of copper as a plumbing material since the time of the Pharaohs. From thermodynamic considerations, Krapp and Mann, 1992 date earliest use of native copper at 7000 to 9000 B.C., copper from ores at 3000 to 5000 B.C. and alloying at 2000 to 3000 B.C. and argue that processing emerged in order of ease of performance. According to the Copper Development Association, plumbing, heating and building wiring are the three most important uses of copper and its alloys; in the US alone (since 1946), more than 3 million miles of copper tubing has been installed in water service and distribution systems for buildings (see review by Anderson, 1986). As a plumbing material, copper is popular, functions well, has a good program of quality assurance, is based on eddy current method, is available during manufacture, and industry has developed techniques that remove the drawing chemicals (Symons, 1986). European developments in the use of plumbing materials are reviewed by Wagner (1986). According to the Minerals Yearbook 1991, mine production of copper reached a record level of 8.8 million metric tons; refined consumption equaled 10.8 million tons (Jolly, 1993; see also Peterson and Cappa, 1993). A glimpse of the long tradition and history of copper mining in part of America is provided in a review of the history and sociology of Lake Superior Copper mines (Lankton, 1991). Copper has a wide range of other beneficial applications by man, including agricultural uses (fungicides, pesticides, nutrient supplements), antifouling applications, wood preservation, medical uses (ranging from anti-cancer and anti-inflammatory drugs to radiopharmaceuticals), and a host of industrial applications. These are discussed in another section of this report.

II.2 ANTHROPOGENIC COPPER - NATURE AND EFFECTS

Metals may be enriched in the environment by natural processes as well as from anthropogenic sources (see review by Vernet, 1992). New attention is being paid to these "natural" sources of "contamination" and their effect on the environment. Volcanic ash from Mount Etna, for example, is enriched with copper by a factor of 1.4; ash from Mt. St. Helens by 2.6 (Cimino and Ziino, 1983a) and metals leached from the ash may be bioavailble (Cimino and Ziino,1992, 1983b and Cimino et al., 1992). Pempkowiak and Szefer (1992) discuss natural sources of copper enrichment in the southern Baltic. Metal concentrations in waters in contact with natural mineral deposits may be enriched by orders of magnitude, even in the absence of mining; such waters can be naturally acidic and have filtered concentrations of Cu as high as 12 mg/L (Runnells et al., 1992). Runnells et al. (1992) point out that these natural concentrations can far exceed the EPA primary and secondary standards for drinking water (1 mg/L for Cu) as well as water quality criteria for the protection of aquatic life. Fauth and Hindel (1988) mapped FGR stream sediments and water to find natural anomalous concentrations of elements. Peuraniemi (1991) found highly localized metal anomalies related to till geochemistry in a survey of southern Finnish soils. The most recently discovered sources of natural metal enrichment are deep ocean hydrothermal zones. Tambiyev et al., 1992 discuss mechanisms for hydrothermal sedimentation and the origin of ancient hydrothermal sediment deposits in a paper on the Guaymas Basin Hydrothermal Zone, Gulf of California.

Separation of anthropogenic from natural source copper can be a difficult process. Williams (1992b) in the conclusion to an interesting paper on diagenetic metal profiles in recent sediments of Loch Ba, Scotland, provides a cautionary note to the interpretation of metal profiles in pollution studies:

> "While acknowledging the impact of anthropogenic activity on the recent loading of elements such as Pb, Zn, and Cu to the Loch Ba catchment ... most available evidence indicates that their down-core profiles are more strongly controlled by the subsurface redox regime than by historical influx variations. At station Ba3, the surficial (post-1840) sediments are enriched, simply because they provide conditions in which upwardly mobile metals from the underlying sequence can precipitate with, or become adsorbed to, hydrous oxides of Fe and Mn. The marked similarity between the resultant enrichment pattern and that of industrially polluted sediments raises the possibility that some diagenetic profiles may previously have been mistaken for cultural features. The implications of such errors could be particularly severe in areas where sediment-based "pollution chronologies" have formed the basis of "causal linkages" between atmospheric deposition and recent lake acidification..."

Identifying the natural background concentrations of elements can be difficult in areas where the "anthropogenic overprint" is very old (Runnells et al., 1992), in England, for example, where copper mining is at least 2000 years old [copper enrichment has been detected in skin samples from of 2000 year old "Bog men" of England due to copper based pigments used as body paints (Pyatt et al., 1991)]. Prager and MacCall (1993) used a biostatistical model to separate contaminant and climate effects in a study of the collapse of the Pacific sardine stock. In many studies, discrete sources cannot be identified, particularly in heavily populated and industrialized, multi-use areas such as estuaries - e.g. Hagen, 1990 (Fraser estuary); Swindlehurst and Johnston, 1991 (Bilbao); Furthermore, estuarine processes are highly complex (see excellent review of estuarine processes by Michaelis, 1991). Generalizations about anthropogenic enrichment patterns should be viewed with caution. Davis, 1993, for example, in a reanalysis of open ocean vs. coastal ocean pollution based on the GESAMP data, does not find support for the "dirty coasts, clean seas" hypothesis. Taylor, 1993, provides a highly critical analysis of the GESAMP programs. One generality which is likely to hold is that water and soils are the ultimate sinks for persistent contaminants (Menzer, 1991) hence the large number of research studies on metal levels in soils, water and sediments.

As point source controls become effective, diffuse sources of heavy metal pollution are gaining in importance (Zabel, 1993). This hypothesis is reinforced by Rang and Schouten (1988) who point out that as a consequence further control measures will only be effective over the long term. Goldberg, 1992, reviews three case studies of chronic pollution events involving heavy metals (one of which was the 1986 'greening' of oysters at a mariculture facility in Taiwan linked to chelated copper from a recycling operation). He argues forcefully that there is an overmphasis upon metals as a cause of environmental problems. Maynard (1990) reviews environmental tests and the elements of variability and discusses the implications for compliance monitoring.

Examples of some recent references to anthropogenic sources of heavy metals to the environment (not all possible sources identified):

Diffuse sources -

Agricultural feed additives - Sarmani et al., 1992

Fertilizers and composts - Hsu and Hong, 1993 (animal manures); Lustenhouwer and Hin, 1993 (Dutch composts)

Fungicides - Alva, 1993; Camoni et al., 1991; Celardin et al., 1992; Kern and Wucherpfennig, 1992b (residual copper in wines); Krause et al., 1992 (spray drift); Schauder and Auerswald, 1992; Yamada et al., 1992b

Pesticides - Chatterjee et al., 1993a (Paris Green - contamination of groundwater in Calcutta); Finlayson et al., 1993 (Sacramento River valley); Spicer and Weber, 1991

Herbicides - Lan et al., 1992

Smelters (dust, runoff from waste piles, input to marine aerosols)- Bagatto et al., 1993;

Non-ferrous metallurgical plants (air pollution) - Dragnev et al., 1991; Remoudaki et al., 1991

Wood preservatives - Cox, 1991 (review); Johnson and Thornton, 1991; Neary et al., 1993 (review); Pohlandt et al., 1993 (leachability of ash from treated woods); Stinson et al., 1992

Antifouling paints (and pressure washing effluents) - Institute Francais de Recherche pour L'Exploitation de la Mer, 1991 (trend to increased copper in mussels and oysters attributed to increased use of copper anti-fouling paints after TBT ban)

Atmospheric deposition and acidic precipitation - Hall et al., 1993; Holsen et al., 1993; Infante et al., 1989 (Ponce, Puerto Rico - anthropogenic inputs very small); Irvine et al., 1989 (Hamilton, Ont., Canada); Mutsch, 1992; Norton et al., 1992; Plichta and Kuczynska, 1991; Plichta et al., 1991; Recynska-Dutka, 1990a,b (Niepolomice Forest, Poland); Veron et al., 1992 (industrial sources for trace elements in N. W. Atlantic troposphere)

Urban runoff, roadways, stormwater; urban building materials - Berndtsson, 1993 (copper roofs); Felstul and Montgomery, 1991; Minoranskij and Wojciechowski, 1991; Vermette et al., 1987

Corrosion and water distribution systems materials - Gotoh, 1993 (atmospheric corrosion of metals and air pollution); Neff, 1986; Schock, 1986 (includes discussion of several corrosion control measures); Shibad et al., 1989; Symons, 1986

Power generation (e.g. coal fired power plants) - French, 1990 (Ph. D. thesis - Severn Estuary)

Point sources -

Mining/ mine spoils/ tailings/ acid mine drainage - Bradley, 1988; British Columbia Acid Mine Drainage Task Force, 1990; Chen, 1992b; Dave, 1992; Karbe, 1988 (review); Kessler, 1991 (Island Copper Mine); Salomons, 1988 (review); Scott and Lo, 1992 (review tailings management)

Sewage outfalls and sludge - Buckley, 1991a; Chander and Brookes, 1991c (sludge as a soil amendment); Johnston et al., 1993; Mattsson et al., 1991; Mignosa and Paoletti, 1992; Prabhakaramurty and Satyanarayana, 1990; Romaña et al., 1992; Sung, 1991 (Boston Harbour); Tkalin, 1992a,b (Sea of Japan)

Dredge spoils - Swindlehurst and Johnston, 1991

Waste reclamation, treatment, recycling - Goldberg, 1992

Waste disposal at sea - Franklin and Jones, 1993; London Office for the Dumping Convention, 1991

Miscellaneous industrial effluents and industrial outfalls - Camusso et al., 1992; Chen, 1992b; Guilizzoni and Lami, 1988 (Lake Orta); Konar and Mullick, 1993; Langston and Pope, 1991; Naimo et al., 1992 (Upper Mississippi River); Ouddane et al., 1992; Owens, 1991; Prabhakaramurty and Satyanarayana, 1990; Tkalin, 1992a,b (Sea of Japan)

Waste landfilling/ storage - Polan and Jones, 1992

Industrial emissions to the atmosphere - Novácek et al., 1990

Port loading/ unloading facilities - Machiwa, 1992 (Dar es Salaam)

Shipbuilding and maintenance; ports - Mecray et al., 1991 (historical); Phillips et al., 1992 (copper slag for sand blasting of ship hulls); Wilson, 1991 (M. Eng. Thesis - discharge of bilge water in Norflok Naval Station Harbor - mass loadings small; minimal impacts)

Offshore oil and gas exploration and production - Cofino et al., 1992

Monitoring and assessment programs and reports from environments affected by anthropogenic metal enrichments

Bioindicators of anthropogenic copper enrichment (based on correlation often observed between metal concentrations in animal and plant tissues and concentrations in the environment)

Terrestrial organisms - Aamlid and Venn, 1993 (Norwegian forests); Alegria et al., 1992 (vegetables); Angelone and Bini, 1992 (W. Europe soils and plants); Berger and Dallinger, 1993 (snails); Blamowski et al., 1991 (Polish vegetables); Józwik, 1990, 1991, 1992 and Józwik and Magierski, 1991, 1992, 1993 (Spitsbergen bryophytes); Keitel and Zimmermann, 1989; Kopeszki, 1991 (soil collembola); Lusky et al., 1992 (game in Schorfheide-Chorin Nature Reserve); Majori et al., 1991a (mussels); Savich et al., 1992a (soil and plants); Schenone and Lorenzini, 1990 (plants); Simkiss and Watkins, 1991 (soil microbes and snails); Turnau, 1990 (fungi); Yoshinaga et al., 1993 (human hair)

Aquatic and marine organisms - Amyot et al., 1992 (St. Lawrence River amphipods); Antoine et al., 1992 (North Sea seabirds and porpoises); Canli and Furness, 1993a (lobster); Clements, 1991 (stream community); Cornwell and Stevenson, 1990 (submerged aquatic vegetation in Chesapeake Bay); Fryer and Nicholson, 1993 (statistical tests to separate trends from sampling variation); Glime, 1992 (bryophytes - review); Guzmán and Jiménez, 1992 (coral reefs); Hendriks and Pieters, 1993 (Rhine delta aquatic organisms - residues of many compounds decreased over recent decades); Jaffe et al., 1992 (corals); Joanny et al., 1993 (sentinal species in French marine littoral); Kaviras (prawns); Koli, 1993 (fish); Landahl, 1992 (NOAA National Benthic Surveilance Program database - west coast fish); Lavie and Nevo, 1991 (marine pollution and population genetics); Nolan, 1991 (Mussel Watch); Pempkowiak and Szefer, 1992 (south Baltic biota); Phillips et al., 1992 (mussels); Phillips and Rainbow, 1993 (review); Richelle-Maurer et al., 1991 (freshwater sponges); Sen Gupta et al., 1989 (metal levels in fish meat from Indian coastal waters suitable for human use despite severe degradation of environment by sewage discharges); Varanasi et al., 1989 (National Benthic Surveilance Project - Pacific Coast - no correlation between metal levels in sediment and fish); Zürn and Müller, 1993 (biosensor)

Soils and sediments are the ultimate environmental sinks for anthropogenic copper conseqently there is great interest in metal levels in these environments

Soil and sediment metal levels - Benes and Benesová, 1992, 1993 (Czech soils); Everaarts and Fischer, 1992 (Dogger); Favarger and Vernet, 1989 (Rhone sediments); Howa and Vernet, 1989 (Leman Lake); Impens et al., 1991 (review of management of contaminated soils); Kersten et al., 1990 (sediments and suspended particulate matter of North Sea); Kratz, 1991a (forest soils in Germany - surface soils a sink); Podlesáková and Nemecek, 1993 and Nemecek and Podlesáková, 1992 (retrospective monitoring of Czech soils - presumed high level of soil contamination was not proved); PTI Environmental Services, 1991 (reference area perfomance standards for Puget Sound); Ruiz and Romero, 1992 (Basque rivers); Seisuma and Legzdina, 1991b and Sen Gupta and Kureishy, 1989 (Gulf of Riga); Shankar and Karbassi, 1991 (Arabian Sea - baseline); Thomas and Goyette, 1989a,b (Vancouver Harbour); Walkusz et al., 1992 (Baltic); Wannemacher, 1991 (Wiesbaden); Zhang, 1991c (Daya Bay, China - baseline); Zhelyazkov et al., 1991 (Bulgarian forest soils)

Records of anthropogenic enrichment inferred from soil and sediment strata - Chester, 1988; French, 1990 (Ph. D. Thesis - Severn Estuary); Guilizzoni and Lami, 1988 (Lake Orta); Trefry et al., 1992 (Manatee Pocket, Fla.); Williams, 1992b

Speciation/ mobility/ sorption/ partitioning of metals in the environment [see discussions and references in other sections of this report] - Fischer and Wartel, 1992; Förstner, 1991 (review); Lim, 1991 (Ph. D. Thesis); Mayers and Beveridge, 1989 (sorption of metals to bacterial cell walls); Ongley et al., 1992 (sediment partitioning); Osuna López et al., 1986; Rauret et al., 1989b; Reczynska-Dutka, 1991; Rees, 1991 (review of transport of contaminants by colloid-mediated processes); Regnier et al., 1990 (suspended matter in Rhone); Rubio et al., 1991; Steinberg and Tayarani-Dastmalian, 1991; Williams, 1992b; Young et al., 1992 (sorption by Trent Channel sediments)

Recently published general reports on state of the environment including conference proceedings, books, reviews, etc. - Hanley and Couriel, 1992 (coastal management issues in the Northern Territory, Australia); Keondjian et al., 1992 (practical ecology of sea regions - review); Kryuchkov, 1991 (the northern ecosystem in Russia); Matsui, 1992 (proceedings - water contamination); Olem, 1993 (lake and reservoir management); Reid et al., 1990 (Toxics Deposition Monitoring Network - Great Lakes); Sen Gupta, 1991 (seas around India); Stebbing et al., 1992 (North Sea); Tkalin et al., 1993 (Vladivostok - marine environment); World Health Organization, 1993b (report on the WHO commission on health and the environment - control of waterborne pathogens identified as prime priority)

Recently published seminar proceedings, reviews, monitoring reports, sediment and water quality reports for specific environments - Arbeitsgemeinschaft fur die Reinhaltung der Elbe, 1992, 1993 (Elbe water quality reports); Arbouille et al., 1989 (Lake Léman); Bonnevie et al., 1993 (New Jersey waterways sediments); Boyd et al., 1989 (Vancouver Harbour sediments); Carbiener and Tremolieres, 1990 (Rhine rift valley groundwater); Chapman, 1992 (Pollution status of North Sea sediments); Dalziel et al., 1993 (Pictou Harbour and East River Estuary, Nova Scotia); Davis et al., 1992 (National Pollutant Discharge Elimination System [NPDES]

Program - San Francisco Bay); Dorgelo and van der Kamp, 1991 (Ijsselmeer); FAO Committee for Inland Fisheries of Africa, 1992; Fauth and Hindel, 1988 (survey of FRG stream sediments and surface waters); Gottholm and Turgeon, 1991 (Gulf of Maine - part of National Status and Trends Program); Halbrook et al., 1991 (Tennessee's East Fork Poplar Creek - biological monitoring as alternative to compliance to water quality standards); Hart and Andrews, 1991 (Great Lakes - In-Place Pollutants Program); Heinz et al., 1992 (Chesapeake Bay wildlife); Lapaquellerie et al., 1992 (Arcachon Lagoon); Lee et al., 1990 (Maxwell Bay, Antarctica); Loez and Salibián, 1990 (Reconquista R., Argentina); Magazzu et al., 1992 (Lake of Ganzirri, Messina); McCreary et al., 1992 (San Francisco Estuary); McMahon (Shannon Estuary - review); Morley et al., 1990 (Gulf of Lions); Munawar and Edsall, 1991 (Upper Great Lakes Connecting Channels); Proctor and Bloome, 1993 (Minnesota stream); Rakusa-Suszewski and Krzyszowska, 1991 (Polish Antarctic station); Salchow, 1992 (North Sea - Dogger); Schönfeld et al., 1990 (German Bight); Seritti et al., 1990 (Mediterranean); Sfriso et al., 1992 (Lagoon of Venice); Sorg and Bell (Chairmen), 1986 (Plumbing Material and Drinking Water Quality - seminar); Stabel et al., 1991 (Lake Constance); Strunk, 1992 (Mosel region); Thomas et al., 1991a (Arctic data compilation - Beaufort Sea); Thomas et al., 1991b (Northwest Passage); Wilken, 1991 and Wilken et al., 1991 (Elbe); Wollast, 1990 (Rhone River less polluted than previously thought)

A number of recent references include some discussion of government regulations and the probable consequence of legislation - Alden and Rule, 1992 (discussion of sediement quality criteria); Baccini and Von Steiger, 1993 (Swiss emission standards - soils); Benes, 1991 (Czech Republic standards for application of industrial composts to soils and control of production of composts); Boydston, 1986 (US E.P.A. drinking water regulations and impact on materials used in water systems); Choudhury et al., 1993 (assessing risk of noncompliance in wastewater treatment); Franklin and Jones, 1993 (U.K. MAFF monitoring to demonstrate compliance with various UK and EU directives regarding disposal of wastes at sea); Grigoryan, 1990 ("maximum permissable concentration" for irrigation water in Russia worked out for soils and crops); Hentz et al., 1992 (EPA perormance standards for sewage treatment plants); Kuchenrither et al., 1992 (impact of proposed US drinking water regulations on sludge); Isom, 1992a (biomonitoring - 4th annual literature review - includes consideration of metals and metals criteria); Ramaley, 1993 (monitoring and control experience under the Lead and Copper Rule - case study); Sorg and Bell (Chairmen), 1986 (drinking water); United States Environmental Protection Agency, 1993a (aquatic life criteria); United States Environmental Protection Agency, 1993b (Tribal water utility management); Wagner, 1992 (copper uptake from domestic drinking water installations after stagnation, especially of low pH water, may exceed German Drinking Water Regulation level of 3 mg Cu/L); World Health Organization, 1993a (health-based provisional guideline value of 2 mg/L for copper in drinking water)

Various recent studies have included assessments of the environmental consequences of a range of pollution abatement programs - Balkas et al., 1993 (Izmer Bay case study in relation to the Mediterranean Action Plan); Bauereis, 1992 (Chesapeake Challenge for Sustainable Development - over 95% point source compliance); Behmanesh et al., 1992 (National Hazardous Waste Survey - incinerated waste streams); Brinkman et al., 1988 (consequences of national water management in the Netherlands); Civili, 1992 (Mediteranean Action Plan - under UNEP - first decade); Calderoni and Mosello, 1990 (Lake Orta); Flegal and Sañudo-Wilhelmy, 1993 (San Diego and San Francisco Bay sediments remain enriched in spite of efforts to control point-source discharges - diagenic remobolization from sediments); Fucik et al., 1991 (Alice Mine); Great Britain Department of the Environment, 1992 (effects of TBT restrictions); Griffiths and Keller, 1992 (Sudbury lakes recovering following emission reductions); Kreis, 1988 (Detroit River, Michigan); Lääne and Wilhelms, 1993 (Second Baltic Sea Pollution Load Compilation); Oten Hulscher et al., 1992 (Rhine emission reduction program); Paulson et al., 1993b (Puget Sound); Keller, 1992, Keller et al., 1992b and Matuszek et al., 1992 (Sudbury lakes); Paalman and van der Weijden, 1992 (Rhine); Stigliani et al., 1993 (Rhine basin - focus on Cd, Pb, Zn); Wood, 1993 (chapter on water quality modeling)

Cleanup, remediation and restoration projects are underway in a range of anthropogenically affected environments. [Further discussion is given in the seciton below on reduction in metal concentration and impact]. Recent reports, including papers on treatments and technologies - Choudhury et al., 1993 (method to determine risk of non-compliance in wastewater treatment); Deans and Dixon, 1992 (metals removal by biopolymers); Gadd, 1992 (review - biosorption); Gómez Bárez et al., 1991a,b (drinking water treatment); Karathanasis and Thompson, 1993 (constructed wetlands for acid mine drainage treatment); Lustenhouwer and Hin, 1993 (Dutch composts leveles); Matsumoto et al., 1992a (wastewater treatment- review); Muraleedharan et al., 1991 (review of biosorption for metal removal and recovery); Nicholson and Safaya, 1993 (restoration of hazardous waste sites - overview); Polan and Jones, 1992 (review to discover alternatives to landfilling and incineration of sludges); Rigas et al., 1991; Summers, 1992 (bioremediation); United States Environmental Protection Agency, 1992 (Superfund Record of Decision - Torch Lake Site, Houghton C., MI); Wong et al., 1993c (management of Hong Kong sediments)

Health assessments and public health assessments for US sites - United States Agency of Toxic Substances and Disease Registry, 1993a,b,c,d

Pollution assessment methods are continually being applied, developed, tested, and revised. Recent papers including bioassay, toxicity and toxicity testing, reviews, health effects - Axelson et al., 1983 (disease risk in copper smelter workers in Sweden); Burgess et al., 1993b,c (contaminated sediments - sea urchin bioassay); Chander and Brookes, 1991b (difficulties with dehydrogenase activity assay in presence of copper in soils); Cooke et al., 1992 (potential risk to wildlife from eating contaminated earthworms - review); D'Aniello et al., 1990 (cephalopod embryos from Bay of Naples); Dauer et al., 1993 and Dauer, 1993 (biological criteria development as adjunct to toxicity testing); Hall et al., 1992; Hawker and Connell, 1992 (coral reefs - derived tolerance level for reefs of 1 ppb Cu); Hummel et al., 1991 (review of genetic effects of pollution); Jones et al., 1985 (seedling growth); Langevin et al., 1992 (genotoxicity using SOS Cromotest); Mårtensson, 1993 (nitrogen fixation assay); Mazidji et al., 1992 (EDTA plus Microtox to distinguish between heavy metal and organic matter toxicity in wastewater samples); National Technical Information Service, 1993i (fresh water fish - published search); Olsson et al., 1992 and Frank et al., 1992a (seals in Swedish waters - metals not a causative factor); Peakall, 1992 (animal biomarkers - review); Phelps, 1993 (mapping with Corbicula toxicity response); Reish et al., 1992, 1993 (effects of pollutants on saltwater organisms - reviews); Roth et al., 1992b; Tölgyessy, 1993 (ecotoxicology of water pollutants); Tubbing et al., 1993a,b (Rhine phytoplankton and bacteria); United Nations Environment Programme, 1988 (GEMS methods and guidelines); United Nations Environment Programme (UNEP)/IAEA/IOC, 1990 (reference methods and materials); Vogt, 1991 (multivariate ecotoxicological mapping);

II.2.1 MINING, SMELTING AND METAL WORKING

Metals are "...one of the foundations for the development of our present affluent society" (Salomons, 1988). The extraction and working of metals can cause environmental effects ranging from physical and chemical changes to the immediate environment to biological effects in environments remote from the source of the metal enrichment. In the introductory paper to a workshop titled, "Workshop on Metals and Metalloids in the Hydrosphere: Impact through Mining and Industry, and Prevention Technology", Salomons (1988) covers physical changes to the landscape, behavior of released metals in the hydrosphere, acid mine drainage, chemical and physical processes affecting metal concentrations (including adsorption), mobility of metals in deposited sediments, biological effects, pollution assessment and rehabilitation. He stresses (p. 16) that the "...impact of metals cannot be studied in isolation from other (changing) parameters in the hydrosphere." Enziminger (1993) reviews metal finishing and processing. The National Technical Information Service, 1993c provides a published search of recent papers on biochemical applications to ore mining and processing. Karbe (1988) reviews the interactions of metals with biota and further discussion is presented in the section of this review on copper and organisms. Recent references on the environmental effects of mining, smelting and metalworking activities are given below, organized broadly into specific areas of interest:

Specific effects of mining and smelting

Baseline studies and Impact Assessments - Cabrera et al., 1993 (Rio Tinto); Careless and Barnese, 1993 (Windy Craggy copper mine); Gardner, 1992 (Westgold BIMA - case study reviews permitting process); Limpenny et al., 1992 (beach disposal of colliery tailings in high energy environment); Pandolfini and Pancaro, 1993 (Metalliferous hills, Tuscany)

Health assessments

Human health effects noted for workers in metal mining production facilities or people living near production facilities - Axelson et al., 1983; Araki et al., 1993 (Japanese gun metal foundary - Pb main effects); Borodulin-Nadzieja and Gosk, 1992 (nervous syndrom in copper miners); Chen et al., 1993e (mortality from lung cancer among copper miners); Gagné and Létourneau, 1993 (residential district near a copper smelter - lead in blood of children); Hosovski et al., 1992 (penicillamine effects on copper smelter workers); Karjalainen et al., 1992 (cancer risk in Finnish smelter workers); Lipatov and Kozlovskii, 1991; Sandström and Wall, 1993 (lung cancer incidence in Swedish copper smelter workers)

Reports of effects on organisms or biological processes (some including considerations of biological availability of the metals) -

Soils - Hiroki,1992 (irrigation with mine catchment water - effects on soil microbial populations); Vangronsveld and Clijsters, 1992 (biological test system to test for bioavailability and phytotoxicity)

Vegetation - Castaneda and Bhuiyan, 1993 (effect of tailings on irrigation of rice); Jones et al., 1985; Lanaras et al., 1993 (wheat growing on ore bodies); Macyk et al., 1990; Shaw et al., 1991 (variability of moss growth on mine spoil); Zhan et al., 1992 (controlled ecosystem experiments on delay of phytoplankton bloom from mine tailings effects); Zhu et al., 1992a (toxicity test of mine wastewaters on algae)

Animals and birds - Hirano et al., 1993 (tests of effect of CuO on rats); Smith and Morris, 1990 (fish assemblage of Ok Tedi, Fly River); Zhu et al., 1992a (toxicity test of mine wastewaters on *Daphnia*)

Observed impacts in specific environments attributed to mines, smelters and metal works -

Gasses, dusts and aerosols including long range transport - Keller, 1992, 1992b (Sudbury - acidification); Kryuchkov, 1991 (degradation of northern environments); Remoudaki et al., 1991 (western Mediteranean); Romo-Kröger and Llona, 1993 (remote Los Andes); Towle, 1993; Vadjic et al., 1991

Soil accumulations of heavy metals - Hyun and Yoo, 1991 (exchangeable copper concentrations low in paddy soils); Komisarek et al., 1990; Minina, 1989; Rachwal et al., 1990 (sequential extraction); Szerszen et al., 1991; Vadjic et al., 1991

Metal accumulation in plants (including reports of hyperaccumulation; tolerance; indicator species) - Andruszczak and Huczynski, 1989; Bagatto et al., 1993; de Koe et al., 1991; Dragnev et al., 1991; Farago and Mehra, 1992; Klein and Vlasova, 1992 (circumpolar North lichens threatened by air pollution); Lukaszewski et al., 1993; Morishita and Boratynski, 1992 (Cu accumulation only in roots near Japanese smelters); Rachwal et al., 1992 (poplar clones with different tolerances)

Metal accumulation in animals - Alikhan, 1993 (isopods); British Columbia Inland Waters Directorate, 1989 (Coumbia River fish); Denneman and Douben, 1993 (Dutch barn owl feathers); Dragnev et al., 1991; Hills and Parker, 1993 (beavers near Sudbury); Kessels and Wensing, 1993 (Dutch cattle); Launer et al., 1991 (German "Black Game"); Morgan and Morgan, 1992 (earthworms); Niemi et al., 1993 (Finnish elk)

Revegetation/ recovery (including studies of metal release from spoils, slags and tailings) - Döring et al., 1992; Macías et al., 1992; Perez and Calvo de Anta, 1992; Seoane et al., 1991; Taylor et al., 1993b; Theiesen et al., 1993; Tümen et al., 1991,1992; Turner and Dickinson, 1993b; Wozny et al., 1992 (search for tolerant plants for revegetation); Whiteley and Williams, 1993; Zhan et al., 1992 (tailings in controlled ecosystem experiment)

Recent reports of effects of metals from mining, smelting and metal working on water and sediment quality (some incuding consideration of metal speciation and bioavailability) -

Water - Bradley, 1988, 1989 (fluvial system - UK rivers mined historically); Di Gregorio and Massoli-Novelli, 1992 (Sardinia - Pb/Zn mine tailings ponds); Luan et al., 1992; Pettersson et al., 1993 (Cu in acid leachates quickly complexed by humic and fulvic acids); Perez and Calvo de Anta, 1992 (toxic levels of metals measured in runoff waters from spoil heaps in Sulphide mine area in Galicia); Scott and Lo, 1992 (optimal tailings management at Highland Valley Copper); Waara, 1992 (Swedish lakes)

Sediments (recent and historically enrichments) - Bradley, 1989; Dave, 1992 (River Kolbäcksån lakes - historical mining and steel works - toxicity related to Cd, Pb, Zn); de Vevey et al., 1993 (bioavailability by metPAD bioassay); Drysdale and Pederson, 1992 (geochemistry of buried tailings deposit in Howe Sound, B. C.); Limpenny et al., 1992 (beach disposal of colliery tailings in high energy environment); Rang and Schouten, 1988 (historically enriched fluvial deposits as source of pollution)

Acid mine drainage - Amacher et al., 1993 (effect of NaOH addition); British Columbia Acid Mine Drainage Task Force, 1990 (review); Karathanasis and Thompson, 1993 (constructed wetlands for remediation of acid mine drainage); Luan et al., 1992

Effects on plants and animals - Indicators and bioaccumulation - Cain et al., 1992 (aquatic insects); Dunn et al., 1992 (B.C. Fucus gardneri); Fuge et al., 1993 (Welsh bivalves); Glooschenko et al., 1992 (amphibians in Sudbury lakes); Jaczwski et al., 1991 (Polish cattle); Johnson et al., 1992b (zoobenthos communities in Swedish lakes - no clear trends relative to smelter); Simkiss and Watkins, 1991 (soil microbes and snails); West et al., 1993a (tests showed that assessment of availability of copper from test sediments dependent on organisms used; sensitivity of organisms not predicted from water-only exposures); Zhu et al., 1992b (algae in Le An River, Dexing Copper Mine)

Recent reports of rehabilitation of mine and smelter impacted areas - Dixit et al., 1992 (recovery of lakes affected by Sudbury smelters); Fucik et al., 1991 (measuring success of reclamation); Geiger et al., 1993 (older Swiss smelter/foundaries - soil reclamation); Komisarek et al., 1990 (liming); Matuszek et al., 1992 (Sudbury lakes); Morgan et al., 1992; Runnells et al., 1992 (points out that "in mineralized areas it may not be scientifically reasonable or technically possible to remediate the water to standards that are lower than the natural background concentrations.")

Treatment processes and metal removal/recovery - Ajmal et al., 1993 (removal from electroplating wastes); Burgstaller and Schinner, 1993 (review - metal winning with fungi); Choudhury et al., 1993 (methodology to determine probability of noncompliance for wastewater treatment plants); Gadd and White, 1993 (review of biosorption and bioprecipitation); Watts and Chapman, 1993 (fungal removal)

Biotechnology in mining (bioleaching) - Bustos et al., 1993 (Lo Aguirre, Chile - first plant to use bacterial thin-layer leaching process)

Bioleaching using bacteria of the genus *Thiobacillus* - De Silóniz et al., 1993; Duarte et al., 1993; Porro et al., 1993; Schroeter and Sand, 1993; Southam and Beveridge, 1993; Tuovinen and Fry, 1993

II.2.2 WASTE MATERIALS INCLUDING SEWAGE, SLUDGE AND WASTEWATER

Waste materials from municipal, industrial and agricultural sources enter the environment chiefly through wastewater and stormwater discharges and outfalls, landfilling, incineration (including ash disposal), ocean dumping and agricultural reuse. All of these practices are subject to increasingly stringent government regulation and each carries with it a unique set of advantages and potential environmental consequences. Domestic sewage sludges, for example, are a valuable source of macro and micronutrients (Mench et al., 1992) and is an important resource for improving impoverished soils. Smith (1992) argues that proposed lower metal limits for composts compared with sewage sludge would be unnecessarily restrictive to compost use. Wastewaters may be a critical source of irrigation waters in countries such as Israel where fresh water is at a premium (Avnimelech, 1993). Because it largely determines metal release from waste such as municipal sewage incineration wasteVan er Sloot et al. (1992) highlight the role of chemical speciation and its significance for leaching tests for decision making. Lowe (1993), in a paper on the development of sludge disposal strategy for the Hong Kong Territories, provides a discussion of the various use and disposal options. Behmanesh et al., 1992 surveyed compositions of incinerated waste streams for the US EPA database. Concern that metals may persist and accumulate in the environment has led to a large number of studies on the long term consequences of such practices as the land application of composts and sludges. Reports of these studies are included in the detailed lists below.

Sludge - reviews - Polan and Jones, 1992

Land application of sewage sludges -

Characterization of sludges - Diez et al., 1991; Domingues et al., 1991b; Ghirardini et al., 1992 (model simulation of heavy metals in treatment plants to predict effluent quality for agricultural disposal); Lin, 1992 (inhibition of methanogenseis by a mixture of heavy metals); Mattsson et al., 1991 (Gothenburg, Sweden - total domestic load = 20-30% for metals); Mehrotra et al., 1993; Monteith et al., 1993 (modeling fate of metals in municipal water pollution control plants); Ottaviani et al., 1991,1993 (chemical and mutaginicity testing)

Accumulation and mobility of elements in soil profiles (includes lysimeter experiments) - Abou Seeda et al., 1992b; Bhoyar et al., 1992; Biddappa et al., 1991; Chen and Zheng, 1992 (loading capacity of soil for pollutants); Chino et al., 1992; Gandais and Marchandise, 1992; Kasatikov et al., 1992, 1993; Liang and Corey, 1993; Lin et al., 1992a (multifactor model of heavy meal release/retention); McLaren and Ritchie, 1993; Olaniya et al., 1992a

Effects of sludge on chemistry and speciation of soil elements - Basta et al., 1993 (model of soil absorption of heavy metals); Campanella et al., 1993; Cavallaro et al., 1993; Kim et al., 1989; McGrath and Cegarra, 1992

Effects of sludge on vegetation and soil fertility including estimates of bioavailabiliy - Abou Seeda et al., 1992a; Angle et al., 1993; Bansal, 1992; Beyer et al., 1992; Brendecke et al., 1993; Calliari et al., 1993; Domingues et al., 1991a; Forge et al., 1992 (protozoan bioassay for bioavailability); Juste and Mench, 1992; Letty et al., 1991; Mench et al., 1992; Piotrowska and Galczynska, 1990; Quinche, 1993; Sachdev et al., 1993; Smith, 1992

Effects on soil microbiology - Brendecke et al., 1993 (does not lend support to using soil microbial activity as index of soil fertility); Chander and Brookes, 1991a,b,c,d,1993 (long term studies); Chaudri et al., 1993a; Hattori, 1992; Obbard et al., 1993

Effects on higher levels of the food chain - Benniger-Truax and Taylor, 1993 (elevating pH levels did not reduce metal transfer to biota); Protz et al., 1993 (earthworm transport); Weber, 1993 (terrestrial chironomids)

Discussions of sludges and government regulations - Chang et al., 1992 (review of methodology for establishing phytotoxicity criteria); Cortés et al., 1992 (EC and Spain); Hentz et al., 1992 (USA EPA); Ontario Ministery of the Environment, 1991 (variability of trace metals in treatment plants - Ont. guideline limit for nitrogen to metal ratio=10 for copper); Portmann and Rowlatt, 1992 (sea disposal)

Toxicity and toxicity testing - Strotmann et al., 1992

Toxicity to ciliates from activated sludge - Abraham et al., 1992; Madoni et al., 1992

Other means of sludge disposal -

Landfilling/stabilization ponds - Cheung et al., 1993 (toxicity of landfill leachates to microalgae due to ammoniacal-N and organics not trace metals); Fukunaga et al., 1992; Gallorini et al., 1993 (trace element determination in industrial waste landfill leachates); Keenan et al., 1993 (treatment of landfill leachate); Loehr et al., 1993; United States Agency for Toxic Substances and Disease Registry, 1993e (public health assessment)

Ocean dumping - Portmann and Rowlatt, 1992 (review - only minor effects generally noted)

Other methods - Chishti et al., 1992 (recovery of sludge protein and use as animal feed supplement)

Solidification/stabilization - Bricka and Jones, 1993; Dusing et al., 1992; Harvey et al., 1990 (glassification)

Metal reduction or removal from sludges -

Bioleaching and biosorption - Blais et al., 1992 (reduction of indicator bacteria by bioleaching process), 1993a,b; Couillard and Mercier, 1993; Jain and Tyagi, 1993; Pümpel and Schinner, 1993 (biosorption with native fungal pellets); Sreekrishnan et al., 1993; Tyagi et al., 1993a,b

Physicochemical methods - Couillard and Mercier, 1992; Gworek et al., 1991 (zeolites); Prairie and Stange, 1993 (photocatalysis)

Composts and agricultural wastes [broiler litter; pig slurry]

Composition/ metal concentration/ speciation/ mobility - Ciavatta et al., 1993 (increase in metal content during composting); García et al., 1991 (heavy metal increase during composting); Japenga et al., 1992 (liquid animal manure - complexation with high molecular weight organic matter); Villar et al., 1993 (copper mainly in available forms - heavy metals and nutrients in composts generally than in animal wastes and greater than or equal to levels in sewage sludge)

Effects on plants/ soil fertility (bioavailability) - Baca et al., 1992 (sugarcane bagasse); Bernal et al., 1993 (pig slurry - most of the micronutrients were immobilized in the soil); Fasidi and Ekuere, 1993 (mushroom cultivation on local cellulosic waste); Henry and Harrison, 1992 (less than 1% copper in soluble form); Kao, 1993 (sawdust swine waste composte increased soil fertility); Nogales et al., 1987 (town compost); Smith, 1992; Smith et al., 1993b (broiler litter)

Effects on higher levels of the food chain - Mueller et al., 1993 (forest soil invertebrates)

Incineration of municipal waste materials

ash - Hinton and Lane, 1992; Schwarz and Stieglitz, 1992; Theelen, 1992 (toxicity testing); Van der Sloot et al., 1992 (leaching tests for decision making - role of chemical speciation is highlighted)

slags - Zavattiero et al., 1992 (metal release relative to secondary use as roadbed material)

Wastewaters - Matsumoto et al., 1992a (Wastewater treatment - review); Yeoman et al., 1993 (metal speciation during treatment)

Irrigation with treated or untreated wastewaters - Abasheeva and Revenskii, 1991; Arora and Chhibba, 1992 (Punjab); Avnimelech, 1993 (Israel - important for water conservation); Ghobrial, 1993 (Kuwait - comparison with government regulations); Kale et al., 1992; Pérez and Gallardo-Lara, 1993 (effects on Zn and Cu availability)

Effects on water - Jop et al., 1991 (source identification - toxicity identification evaluation using Daphnia)

Effects on vegetation - Inglés et al., 1992 (bioavailablity to tomatoes)

Toxicity and toxicity testing and bioassays - Bitton et al., 1992b (MetPAD bioassay); Pérez-García et al., 1993

Techniques for metal removal - Kumawat and Dubey, 1991 (Sorghum straw); Monbouquette et al., 1993 (biomimetic metal sorbing vesicles); Nagendra Rao et al., 1993 (biosorption); Panchanadikar and Kar, 1993 (bioprecipitation); Wang and Srinivasan, 1993 (novel integrated treatment for coal wastewaters); Wong and So, 1993 (removal with Pseudomonas putida)

Effects of sewage/ waste disposal on the marine and aquatic environments - Johnston et al., 1993 (review of 'realistic environmental protection'); Mignosa and Paoletti, 1992 (simulation model for persistant pollutant discharges to low recirculation waters); Shieh and Duedall, 1992 (review - tropics)

Outfalls and water quality - Poulton, 1992 (Bay of Quinte, Ontario - STP loading=730 g Cu/day; industry total loading=453 g Cu/day); Romaña et al., 1991; Wang et al., 1993c (South San Francisco Bay water quality and load allocation model - reduction of point source copper to 2.9µg/L and non-point sources by 50% causes most rapid decline in copper concentrations); Xanthopoulos et al., 1992

Bioaccumulation by marine and aquatic organisms and other biological effects - Carvalho and Lacerda, 1992 (heavy metals in biota of Guanabara Bay lower than expected - postulated due to burial of heavy metals in anoxic sediments, therefore unavailable); Gaston and Young, 1992 (benthos of Louisianna estuary including food chain effects); Güven et al., 1993; McMahon, 1990 (Shannon estuary); Sen Gupta et al., 1989 (metals in fish meat of Bombay area fit for humans despite severe degradation of coastal waters by over 50 years of untreated sewage discharges); Varanasi et al., 1989 (National Benthic Surveillance Project: Pacific Coast)

Sediments - Buckely and Winters, 1992 (Halifax Harbour, Canada - one of the most contaminated marine areas in industrialized world); Contu et al., 1992 (natural wetland); Rodger et al., 1992 (Garroch Head dumpsite); Saeki et al., 1993a; Tkalin, 1992a (Sea of Japan); Wong et al., 1993c (Hong Kong)

II.2.3 REDUCTION OF METAL CONCENTRATION OR IMPACT

The potential cumulative toxicity of many heavy metals (e.g. Donahoe, 1992) has led to the legislation of discharge restrictions by virtually all industrialized countries (Dejack, 1989). Considering also the escalating cost of hazardous waste disposal, researchers are actively developing new waste reduction technologies for reducing metals in wastewater streams because of their potential toxicity to process microogranisms (Hardoyo et al., 1991). Copper increases the removal efficiency of hydrocarbon organic compounds when used as a catalyst on liquid phase oxidation of industrial wastewaters (Chang et al., 1993a). CuCl may be used in extraction and separation of high sulfur coal (Olesik, 1990, 1992) and Hill et al. (1993) describe the development of a novel Cu-based sorbent for removal of H2S from flue gas. Heavy metals were required in the culture medium of a microalgal pond system for removal of CO2 (Negoro et al., 1992). Summers (1992) reviews metals in bioremediation and Enziminger (1992) includes discussions of recover and waster minimization technologies in his review of metal finishing and processing. A published bibliography on recycling of metal scrap is available from National Technical Information Service (1993g). Both biological and physicochemical means of metal removal have been shown to be effective (see comparisons by Rulkens, 1992; Wilde and Benemann, 1993). Recent publications on various aspects of heavy metal removal and recovery include:

Bioremediation

Biosorption - Muraleedharan et al., 1991 (review)

Bacterial, fungal or moss biomass - Becker et al., 1992; Burgstaller and Schinner, 1993 (review); D'Avila et al., 1992 (activated peat); de Rome and Gadd, 1991; Gadd, 1992, (extensive review); Gadd and White, 1993 (review); Grapelli et al., 1992; Lepp, 1992 (review); Mattuschka and Straube, 1993 (Streptomyces noursei waste biomass from pharmaceutical industry); Nagendra Rao et al., 1993 (waste fungal biomass from food and pharmaceutical industries); Nandan and Raisuddin, 1992 (review); Panchanadikar and Kar, 1993; Pümpel and Schinner, 1993; Rizzo et al., 1992; Springael et al., 1993; Wang et al., 1992c; Watts and Chapman, 1993; Wong and So, 1993; Yazgan et al., 1992; Zhou and Banks, 1991, 1992

Free or immobilized algal cells - Mahan and Holcombe, 1992a; dried seaweed biomass - Ramelow et al., 1992a; Wilde and Benemann, 1993; Wong and Pak, 1992; Wong et al., 1993d; Zolotukhina et al., 1992 (Laminaria thalli)

Vascular plants - Mishra et al., 1991 (water hyacinth)

Biosorbents from agricultural byproducts and wastes - Ammar et al., 1993 (fermented bagasse); Bryant et al., 1992 (red fir sawdust);Kumawat and Dubey, 1991 (sorghum straw); Low et al., 1993 (oil palm fibres); Tare et al., 1992 (Xanthate from corn starch)

Biopolymers - Chen et al., 1993c; Mokhtar et al., 1991

Constructed wetlands - Karathanasis and Thompson, 1993

Bioleaching (generally with bacteria of the genus *Thiobacilli*) -Blais et al., 1993a,b; Bustos et al., 1993 (review); Couillard and Mercier, 1993; De Silóniz et al., 1993; Duarte et al., 1993; Groudev and Groudeva, 1993; Jain and Tyagi, 1993; Ostrowski and Sklodowska, 1993; Porro et al., 1993; Pronk et al., 1992; Schroeter and Sand, 1993; Tuovinen and Fry, 1993 (review); Tyagi et al., 1993a (municipal sludge)

Metal removal by physico-chemical methods - Barg et al., 1993; Chishti et al., 1992; Clifford, 1992 (Soxhlet extraction); Couillard and Mercier, 1992 (FeSo4); Deans and Dixon, 1992 (chelation ion exchange); Fane et al., 1992 (ultrafiltration and ion-complexing polymers or ion exchange-resisns); Foster et al., 1993 (TiO2); Haas and Polprasert, 1993; Jaffar and Ehsan, 1993 (granular activated carbon); Laintz et al., 1992 (supercritical fluid extraction); Luan et al., 1992; Prairie and Stange, 1993 (photocatalysis - Cu not easily treated this way); Prairie et al. (TiO2); Rayner et al., 1990 (Chelex); Ritz and Jekel, 1992; Simon, 1993 (supercritical fluid extraction); Yuan et al., 1992

Metal removal with non-biological sorbents - Ajmal et al., 1993 (Fe(III) hydroxide); Das and Bandyopadhyay, 1992 (vermiculite); De Boodt, 1991 (aluminosilicate derivatives); Ho, 1992; Walter et al., 1993 (FloMag products); Monbouquette et al., 1993 (biomimetic metal absorbing vesicles); Wilczak and Keinath, 1993 (activated carbon)

Zeolites - Baidina, 1991; Flytzani-Stephanopoulos et al., 1993; Gworek et al., 1991

Solidification/stabilization with inert binders - Cocke et al., 1991; Dusing et al., 1992; Lin et al., 1993b; McIsaac, 1993; Madany et al., 1991; Ortego, 1992

Novel alternatives to disposal - Collins et al., 1993 (artificial reef construction); Fazekas et al., 1993 (manufacture of trace element feed supplement from industrial waste); Homziak et al., 1993 (oyster cultch); Van Dijk and Wilms, 1991 - waste treatment without waste materials - pellet reactor clean technology (solid grains for industrial use as a by product)

Reclamation and restoration of waste sites - Geiger et al., 1993; Nicholson and Safaya, 1993 (remedial design); Skei, 1992 (review of assessment and remediation strategies for hot spot sediments)

In-place cleanup and bioremediation - Mar et al., 1993 (risks of removing soils near ASARCO copper smelter); Pardieck et al., 1992 (review of hydrogen peroxide use in soils and aquifers)

Soils - Lageman, 1993 ("electrokinetic fencing"); New Brunswick Dept. of Environment, 1993 (soil washing); Stinson et al., 1992 (EPA SITE demonstration: BioTrol soil washing)

Surface/groundwater - Amacher et al., 1993 (liming); Morgan et al., 1992 (H_2S precipitation)

Sediment - Rittle et al., 1993; Yu and Klarup, 1993 (sediment extraction kinetics)

Monitoring and modeling of remediation or reduction - Bumgardner et al., 1993 (stochastic analysis of probability of compliance with water quality objectives*); Wang et al., 1993c (model of water quality effects of load reductions to San Francisco Bay); Winger et al., 1993 (effect of reduced discharge)

Heavy metal residue removal from wines - Kern and Wucherpfennig, 1991; 1992a,b; Kern et al., 1992a,b,c; Sarishvili et al., 1992; Wucherpfennig, 1992a, b

*Bumgardner et al(1993) used Monte Carlo simulation techniques to assess POTW compliance with statistically based water quality objectives. Because mass loadings from the plant are a small percentage of the total from upstream sources, current plant discharges and the expected discharges after retrofitting with a $1 billion treatment system (lime and reverse osmosis) would exceed water quality objectives for Cd, Cu, Hg, and Zn (now) and Cu and Hg (after retrofitting).

II.2.4 ANTHROPOGENIC COPPER FROM INDUSTRY AND AGRICULTURE

Anthropogenic metals may enter the environment as a byproduct of industrial and agricultural activities. Metal enrichment due to these activities is not a new phenomenon. Sediments, for example salt marsh deposits in the Severn Estuary, England, (studied by French, 1993a) carry the record of enrichment and clearly show a post-industrial and pre-industrial pattern of enrichment. Contemporary sediment metal levels also show localized effects of small-scale industry and port activity across the estuary. Similarly, variations in industrial discharge levels over a wider area (in this case the west Cumbria coast) may be detected in surveys of metal levels in biota (effects are generally localized within a few Km of an outfall) (Langston and Pope, 1991). Recent references on various aspects of industrially and agriculturally introduced metals include:

Levels of metals in agricultural materials - Camoni et al., 1991 (commercial fungicides); Dankiewicz et al., 1992 (trace element fertilizers); Handreck, 1993(coir dust as soil additive); Luther, 1993 and Luther and Dudas, 1993 (phosphogypsum fertilizer and leachate); Wolski and Gawecki, 1992 (fertilizer)

Detectable metals enrichment of terrestrial environments from industry and agriculture

Metals in runoff water - Quek and Förster, 1993 (runoff from different roofing materials)

Metals in soils - Bansal et al., 1992 (irrigation with industrial wastewater); Benes, 1991 (industrial composts); Celardin et al., 1992 (Swiss soils); Czarnowska, 1992 and Czarnowska and Gworek, 1991 (Lodz, Poland); Grzebisz et al., 1993 (long term application of farmyard manure fermented with lime and clay); Moreno and González, 1992 (S. W. of Madrid); Tai, 1991 (Chinese paddy soils); Zhelyazkov et al., 1991 (Bulgarian forest soils)

Metals in vegetation - Alva, 1993 (CuS04 in orange orchards); Hashem, 1993 (mycoflora in industrial Yabu City, Saudi Arabia soils); Hsu and Hong, 1993 (copper accumulation from hog manure application); Miszalski and Niewiadomska, 1993 (lichens as indicators); Moreno and González, 1992 (S. W. of Madrid); Rao and Dubey, 1992 (Indian tropical plants); Turnau and Kozlowska, 1991 (fungi in Niepolomice Forest)

Metals in animals - Krelowska-Kulas, 1992c (lambs in agricultural vs. industrial areas)

Metals in foods - Kolczak, 1989 (agricultural products from protective zone of the Huta Kotowice works); Redl, 1992 (Copper in wines from fungicide residues); Samara et al., 1992 (food plants from industrialized area of Thessaloniki, Greece); Son and Son; 1991 (cow's milk - carry over from feeds); Zafaralla and Mangaban, 1990 (Spirulina as a nutrient supplement - grown in cow manure medium)

Detectable metals enrichment of marine/aquatic environments from industrial and agricultural sources

Fresh water - Calderoni and Mosello, 1990 (Lake Orta, Italy); Camusso et al., 1992 (Lake Orta, Italy); Chatterjee et al., 1993a (industrial contamination of an aquifer in India);

Guilizzoni and Lami, 1988 (Lake Orta, Italy); Sarmani et al., 1992 (Malaysia-Linggi R; Cu loading linked to CuSO4 pig feed additive)

Biota - Naimo et al., 1992 (Mississippi freshwater mussels)

Sediments - Deely et al., 1992 (Waiwhetu Stream, N. Z.); Williams, 1992b (potential for misinterpretation of stratigrphy due to diagenic processes)

Marine and estuarine- Al-Sayed et al., 1992 (hypersaline pit - Barhrain); Botnen et al., 1992 (no effect seen from outfall of seawater scrubber at oil refinery in Norway after 18 mos. use); Cohen et al., 1993 (Israeli estuary); Ouddane et al., 1992; Wong, 1993 (Hong Kong)

Biota - Khan and Weis, 1993 (mummichog in polluted tidal creek, Linden, N. J.); Langston and Pope, 1991 (W. Cumbria coast); Paez-Osuna et al., 1993 (clams in N. W. Mexican lagoon affected by agricultural drainage)

Sediments - including stratigraphic analysis to analyze historical trends and identify sources - Bonnevie et al., 1993 (Newark Bay, N. J.); French, 1993a (Severn Estuary, U. K.); Mecray et al., 1991 (Pettaquamscutt River); Morse et al., 1993 (Galveston Bay); Paalman and van der Weijden, 1992 (2.7% Cu input in suspended matter to the Rhine at Rotterdam from industrial sources)

Specific biological effects of industrial materials and effluents -

Effects on plants and animals - Bíres et al., 1991a,b, 1992, 1993 (sheep); Davis-Carter and Sheppard, 1993 (fire ants); Grapentine, 1992 (depressed growth of freshwater clams); Havránková et al., 1993a,b; Launer et al., 1992 (livestock); Washington, 1991 (effect of Bordeauz mixture on apricots)

Toxicity testing - Abdel-Hamid et al., 1993 (algae); Bozsik, 1991b; Cox, 1991 (review of toxicology of CCA); Jop et al., 1991 (Toxicity Identification Evaluation Programs); Konar and Mullick, 1993 (toxicity of mixtures); Laurén, 1991 (fish gill - toxicity of pulp mill effluents); Smith and Papacek, 1991 (copperoxychloride nontoxic to predatory mite)

Reported human health effects - Gailey and Lloyd, 1993 (epidemiology of respiratory cancers in central Scotland); Motolese et al., 1993 (contact dermatitis in ceramics industry - one case of sensitivity to red copper oxide)

Treatment and removal technologies -

Angelov et al., 1993; Bryant et al., 1992 (sorption of heavy metals by untreated red fir sawdust); Dejak, 1989 (case histories of successful waste minimization in the metal finishing industries); Haas and Polprasert, 1993; Lee, 1993 (review); Stinson et al., 1992; Wong and Pak, 1992 (electroplating wastewater treatment with immobilized microalgae)

II.2.5 COPPER FROM DREDGED SEDIMENTS

The necessity of dredging to maintain navigable harbours and waterways produces hundreds of millions of tons of spoil annually which must be maintained or disposed of in an environmentally sound manner (London Office for the Dumping Convention, 1991 - review of its first decade). Some dredged material is enriched with metals.

Monitoring reports of dredging and dredge material disposal - Cofino et al., 1992 (comparison of environmental quality monitoring methods for the offshore); Niedzwiecki and Chinh, 1991 (dumping areas near shipping land Swinoujscie-Szczecin); Shao and Qingxiao, 1991 (Da Yao Bay); Tkalin, 1992b (Sea of Japan); Walkusz et al., 1992 (Gotland Deep)

Toxicity testing and evaluation - Zhang et al., 1992a (enclosed ecosystem study of metal release from sediments)

Bioavailability/ chemistry - Calmano et al., 1992 (chemical mobility and bioavailability of heavy metals from dredged sediments evaluated experimentally); Greig and Pereira, 1993 (lobster and whelk from dump sites in Long Island Sound)

Treatment/ remediation - Fukunaga et al., 1992 (leachates from sludge disposal pond); Martin and McCutcheon, 1992 (overview of processes affecting contaminant release from disposal facilities); Wong et al., 1993c (disposal options for contaminated sediments)

II.2.6 COPPER FROM TRANSPORTATION AND POWER SOURCES

Elevated metal levels from sources related to transportation and power generation (including the effects of acidic precipitation) have been reported in a variety of terrestrial, marine and aquatic environments. Recent reports include:

Copper deposition around roadways

Measurements of copper in runoff and roadside soils - Hewitt and Rashed, 1992 (runoff from major rural highways in New England - 70% Cu in particulate phase); Howard and Beck, 1993 (groundwater contamination by deicing chemicals); Irvine et al., 1989 (Hamilton, Ont.); Kartal et al., 1993 (Turkey); Kratz et al., 1989 (forest edge, Avus Highway, Berlin); Minoranskij and Wojciechowski, 1991 (copper enrichment in soil, plants and beetles from roadsides); Vermette et al., 1998 (urban sediments); Xanthopoulos et al., 1992; Yousufzai, 1991 (Karachi)

Effects on biota - Andrzejewska et al., 1990 (dandelions and herbiverous moths - metal transfer); Bykov and Lysikov, 1991 (mole holes near roadways accumulated heavy metals); Krzysztofiak, 1991 (ant hill soil and ant body copper dropped near roadways); Mariño et al., 1992 (Spanish earthworms); Minoranskij and Wojciechowski, 1991 (copper enrichment in soil, plants and beetles from roadsides)

Remediation - Felstul and Montgomery, 1991 (modeling detention basins); Hsu and Chou, 1992 (identification of tolerant grass species along roadsides in Taiwan)

Waste from energy production and impacts from production facilities

Hazard assessments - Dwivedi and Singh, 1993 (model predicting adverse health effects from coal based power plants)

Biotic effects and impact assessments - Clements et al, 1992 (coal fired power plant - Clinch R., Va. benthic community); Huang et al., 1991a (coral bleaching near nuclear plant outlet related to thermal and light stress not to heavy metals); Johannessen et al., 1992 (marine environment around Statoil Mongstad Oil Refinery, Norway - sediment heavy metals within normal range); Ólafsson, 1992 (Nesjavellir hydrothermal field, Iceland); Stewart et al., 1992 (U. S. DOE's Y-12 Plant in Oak Ridge - stream vegetation)

Ash including fly ash (waste product from burning of coal) - Hamilton et al., 1993 (testing of ash concrete effects on two marine species); Kawecki and Tomaszewska, 1991b, Kawecki et al., 1991a,c (effects of coal ash on orchard plants); Khandkar et al., 1993 (fly ashes sufficient in available Cu to use as a soil amendment); Kress, 1993 (experiments predict no leaching of Cu from deep sea disposal site for coal fly ash); Menon et al., 1993 (leaching from ash amended soils); Singh et al., 1991 (effects on growth of tomato plants, nematode populations and available nutrients in soil); Steele et al., 1992 (chemoattraction of crayfish affected by fly ash slurry)

Revegetation/ treatment technologies - Kolár and Pezlarovà, 1990 (thermal plant ash dump)

Energy exploration - Gee et al., 1992 (German Bight - little effect of metals on meiobenthic community structure - any changes were likely obliterated by massive sediment deposition by Feb. 1990 hurricane); Vidakovic et al., 1993 (toxicity testing of waste drilling fluids)

Acidic Precipitation from all sources

Environmental impacts - Gerhardt, 1993 (review of impacts on stream invertebrates; includes consideration of influence of pH on metal speciation); Ontario Ministry of the Environment, 1990 (Ontario - extensive data report includes measured metal levels)

Aquatic environment - Glooschenko et al., 1992 (amphibians in Sudbury region ponds); Griffiths and Keller, 1992 (benthic recovery in Sudbury lakes following emission reductions); Hall et al., 1993 (pulse of metals in acid precipitation in Chesapeake Bay exceeded EPA 1987 chronic water quality criteria); Hickie et al., 1993 (toxicity tests of trace metal mixtures to alevin rainbow trout and larval flathead minnows); Keller, 1992, Keller et al., 1992b and Matuszek et al., 1992 (recovery of Sudbury lakes - no clear temporal trends in 1980s for Cu, Ni and Zn concentrations); St. Louis et al., 1993 (transfer of metals from acidified lake to tree swallow nestlings); Vesely et al., 1993 (Czech Lake Certovo - copper accumulation rate in sediments rose dramatically about 1640 A. D. although there is no local ore body); Wesson et al., 1991 (Atlantic salmon in acidified rivers)

Vegetation and forests including air pollution monitoring with indicator species - Kratz, 1991a,b (Grunewald, Berlin); Lawrey, 1993 (lichens - Maryland and Virginia - encouraging signs of improved air quality - marked reductions in metals except Al in recent collections); Lukina and Nikonov, 1991 (Kola Peninsula spruce stands); Novácek and Matovic, 1992 (Beskydy Mountains, Poland); Schaug et al., 1990 (multivariate analysis of moss monitoring samples in Norway); Schenone and Lorenzini, 1990 (review); Schmid-Grob et al., 1992 (biomonitoring with moss in Switzerland) pH and metal speciation and bioavailability - Gensemer et al., 1993 (showed trace metal bioavailabilty can affect pH tolerance in diatoms); Matschullat and Wyrobek, 1993 (simulated acidification - metal remobolization from lake sediments)

Treatment technologies and management - Kratz et al., 1991 (liming of pine-oak stands, Gruenewald, Berlin); Livengood and Markussen, 1993 (flue gas treatment technologies)

Anthropogenic copper enrichment of aquatic/marine environments from transportation - Al-Sayed and Madany, 1992 and Madany and Raveendran, 1992 (copper blasting grit from Bahrain shipyards - substitute for sand for ashphalt or as mortar in precast concrete blocks); Weis et al., 1993 (CCA metals from marinas- especially in low energy environments - can accumulate in nearby sediments but may be mostly tightly bound to fine sediments).

III - COPPER SPECIATION, METAL BIOAVAILABILITY AND METAL-METAL INTERACTIONS

III.1 COPPER SPECIATION

References dealing with copper speciation provide important information about metal bioavailability and toxicity as well as the nature of the metal in various environments and the changes that occur over time and under different environmental conditions (Fischer and Wartel, 1992; Olszowka et al., 1992). Several references provide general reviews of the environmental chemistry of copper (e.g. Adriano, 1992; Morel and Hering, 1993) while others review metal speciation and toxicity (Florence et al., 1992a; Sadiq, 1992) or the assessment of techniques to estimate soil (e.g. Häni, 1993) and water quality (e.g. Bumgardner et al., 1993; Symader, 1993). Several review techniques to estimate metal speciation (e.g. Chakrabarti et al., 1993; Dudley et al., 1993; Rauret et al., 1989) or the fate of anthropogenic metals (e.g. Wong et al., 1992). Chemical properties and processes are often specific to the environment and although the effects are reviewed elsewhere, several are included in this section. These include Giusti et al. (1993), on the solubility and partitioning of atmospherically-derived trace metals, Windom et al. (1989), on trace metal-nutrient relationships in estuaries, and Sjöström and Qvarfort (1992), on changes in soil chemistry in central Sweden. A number of efforts have been made to identify the concepts about and processes affecting metal chemistry in natural environments (e.g. Krznaric et al., 1992; Simon et al., 1992; Sposito and Blaser, 1992; Wang et al., 1993c) as will be seen in the list of papers in this section of the review.

Recent references that include discussions of copper speciation are given below:

Atmosphere

- Aerosols - Hamilton-Taylor et al., 1993
- Pollution - Gotoh, 1993
- Precipitation - Lim, 1991 (Ph.D. thesis)

Freshwater (except benthic sediments)

- Lake water - Camusso et al., 1992; Corvi & Khim-Heang, 1989
- River water - Vymazal, 1989
- Reservoirs and ponds - Das & Kaviraj, 1992; Reczynska-Dutka, 1991

Marine (except benthic sediments)

- Anoxic basins - Lewis & Landing, 1992
- Coastal waters - Paulson et al., 1993a; Riso et al., 1993; Sung, 1991; Wu et al., 1990

Estuaries (including tidal zone of rivers) - George, 1993; Michaelis, 1991; Regnier & Wollast, 1993; Regnier et al., 1990; Shao & Wang, 1992

Open ocean (or sea) - Saager et al., 1993; Tsunogai et al., 1982

Miscellaneous - Jones, 1992 (effect of phytoplankton blooms on water quality); Li et al., 1992a,b (metal in large enclosures); Saager et al., 1993 (anoxic brines); Tambiyev et al., 1992 (hydrothermal zone); Xu et al., 1992a (metal in large enclosures)

Benthic Sediments

Review article - Chester, 1988

Estuarine sediments - de Lourdes da Silva Leal & de Luca Rebello Wagener, 1993; Hanson et al., 1993

Freshwater - Klavins et al., 1992b; Larumbe & Casado, 1989 (reservoir sediments); Lin & Huang, 1992; Ongley et al., 1992; Pardo et al., 1993; Rauret et al., 1989b; Rubio et al., 1991; Saeki et al., 1993b; Ye et al., 1991

Saltwater - Abu-Hilal, 1993; Ciceri et al., 1992; Gerringa et al., 1991; Hanson et al., 1993; Páez-Osuna & Osuna-López, 1989, 1992; Takematsu et al., 1993

Miscellaneous - Allen et al., 1993 (acid-volatile sulfide-bearing sediments); Ankley et al, 1993a (role of acid-volatile sulfides in toxicity of freshwater sediments); Das & Kaviraj, 1992 (seasonal variation in the partitioning and bioavailability of copper and zinc in four pisciculture ponds); Jackson et al., 1992, 1993 (role of sediment pH and redox potential in determining metal bioavailability); Karlsson & Brandberg, 1993 (pore water in solid waste sediments); Wallmann et al., 1993 (anoxic, sulfide-bearing sediments)

Soils

General - Bolt et al., 1991; Pardieck et al., 1992

Metal uptake by soils - Du, 1992; Halen et al., 1991; Varshal et al., 1992; Zhu & Alva, 1993b

Mobility of metals in soil - Hogg et al., 1993; Olaniya et al., 1992b; Parmar & Gupta, 1992; Savich et al., 1992b; Selim et al., 1990; Wu & Lu, 1991; Zhu & Alva, 1993e

Soil properties and metal speciation - Diaz et al., 1992c; Keller et al., 1992a; Komisarek et al., 1990; Kovacs et al., 1994; Kratz et al., 1991; Kuiters & Mulder, 1993a; Kuczynska & Choromanska, 1983; Lee & Liao, 1992; Madrid & Diaz-Barrientos, 1992; Raghupathi & Vasuki, 1991, 1992

Soil metal extractability - Biddappa et al., 1991; Lee et al., 1991b; Li & Mahler, 1993; Shan & Chen, 1993; Wu & Selmer-Olsen, 1992

Agriculture practices and soil metal content/speciation - Castro et al., 1992b

Miscellaneous - Bansal, 1992 (metal concentrations with sewage sludge use); Cavallaro et al., 1993 (sewage sludge effect on properties of acid soils); Davis-Carter & Sheppard, 1993 (redistribution of metals by fire ants); Liang & Corey, 1993 (redistribution of sludge-borne cadmium, copper and zinc in a cultivated plot); Obukhov & Popova, 1993 (seasonal dynamics and spatial variability of heavy metal content of soils and groundwater)

Humic substances - products of plant degradation that are found in soils and water. Many of these chemicals complex metals and are important in the chemistry and biological availability of copper.

General - MacCarthy & Perdue, 1991; Mountney & Williams, 1992 (computer simulation of metal ion - humic and fulvic acid interactions; based on work with copper but primarily with nickel); Senesi, 1992 (spectroscopic approach to investigating metal-humic substance interactions)

Water - Machado & da Silva, 1993; McKnight, 1991; Pitter, 1993

Soils and groundwater - Alberts et al., 1992; Finger & Klamberg, 1993; Machado & da Silva, 1993; Oden et al., 1993; Sekulic, 1990a,b, 1991

Humic substances and mine deposits - Pettersson et al., 1993

Miscellaneous - Rate et al., 1992, 1993

Copper and sludge/waste from treated and untreated domestic and industrial materials

Municipal waste - García et al., 1991

Domestic sewage sludges - Bansal, 1992; Campanella et al., 1993; Cavallaro et al., 1993; Jain & Tyagi, 1993; Liang & Corey, 1993; Monteith et al., 1993; Sreekrishnan et al., 1993; Tyagi et al., 1993b; Yeoman et al., 1993

Miscellaneous - Wilson, 1991 (Ph.D. thesis on the environmental impacts from bilge water discharge)

Miscellaneous chemical interactions of copper - Nord et al., 1993 (spionkopite, a copper alloy corrosion product from a 1676 ship wreck); Scarano & Bramanti, 1993; Tsai & Weber, 1992; van den Berg, 1992; Voelkel & Szymanowski, 1993

Use of organic materials to remove (or concentrate) copper from water - Burba & Blödorn, 1992; Burba et al., 1993; Elbaz-Poulichet et al., 1990; Wilczak & Keinath, 1993

Byproducts of copper mining and metal working - Amacher et al., 1993; Bajracharya & Barry, 1993; Hyun & Yoo, 1991; Karathanasis & Thompson, 1993; Macías et al., 1992; Rachwal et al., 1990; Theisen et al., 1993

Analytical techniques (see introductory sections to metal levels in the environment).

III.2 BIOAVAILABILITY

Over the last few years it has become increasingly apparent that both the nutritional and the environmental factors affecting metal bioavailability are being seriously considered. This includes the biogenic effects on metal bioavailability (e.g. Jones, 1992), metal-metal interactions (e.g. Swinkels et al., 1993) as well as the relationship between environmental chemistry and copper. Biochemical factors affecting the activity of copper can also be included under bioavailability because they play important roles in the numerous biochemical reactions that involve copper (e.g. Sahbaz and Somer, 1993; Smith and Valentina, 1993). Outstanding references such as that by Hudson and Morel (1993), on the importance of metal coordination kinetics, provide the basis for an understanding of the dynamics associated with metal bioavailability. The use of this information is becoming widespread and will provide a better understanding of a range of metal-related topics, including nutrient chemistry (e.g. Sahbaz and Somer, 1993) and metal transfer in food organisms (e.g. Amiard-Triquet et al., 1992) to fungicidal activity (e.g. Gerritse et al., 1992) and the environmental fate as well as impact of copper (e.g. Ongley et al., 1992). There is continuing work on the development of techniques to measure either metal bioavailability or, more generally, the complexing capacity of water and soils (e.g. Ge et al., 1992; Iyer and Sarin, 1992). General information on metal bioavailability is found in recent texts and reviews (e.g. Adriano, 1992; Florence et al., 1992a; Meador et al., 1993; Morel and Hering, 1993; Xu et al., 1992a).

Recent references dealing with copper bioavailability in environmental materials include the following:

Metal availability in sediments and soils (includes references that discuss the relationship between metal content of soils and plants) - Agafonov, 1991; Alegria et al., 1992; Aluko, 1993; Angelone et al., 1993; Burgess et al., 1993c (effect of contaminated marine sediments on metal effect in the water column); Calmano et al., 1992; Castro et al., 1992b; Choudhari, 1992; de Kreij et al., 1993; Diaz et al., 1992c; Dynia & Filho, 1993; Hogg et al., 1993; Hopmans et al., 1993; Houba et al., 1992; Komisarek et al., 1990; Kratz et al., 1991; Kuiters & Mulder, 1993b; Neite et al., 1991; Osuna López et al., 1986; Prasad et al., 1991; Raese, 1992; Raghupathi & Vasuki, 1992; Schubauer-Berigan et al., 1993; Sutaria et al., 1992; Thomson et al., 1993; Watanabe, 1992; Wu et al., 1992c; Yu et al., 1991b; Zhu & Alva, 1993a,c

Mine spoils and effluent-affected waters - de Koe et al., 1991; de Vevey et al., 1993; Taylor et al., 1993b; Vangronsveld & Clijsters, 1992

Soils treated with sewage sludge or municipal wastewater - Bansal et al., 1992; Benninger-Truax & Taylor, 1993; Bernal et al., 1993 (nutrient balances in calcareous soils after application of pig slurry); Inglés et al., 1992; Kim et al., 1989; McGrath & Cegarra, 1992

Effects of acidification on metal availability - Albers & Camardese, 1993

The application of information about copper bioavailability is towards an understanding of the requirements for and effects of copper on plants, animals and humans. Recent biological, agricultural and nutritional references containing information about metal availability (and lability) include:

General - Vangronsveld & Clijsters, 1992 (biological test system for evaluation of metal phytotoxicity and immobilization by additives in metal-contaminated soils)

Copper and microorganisms
- Effect of elevated levels of copper - Chao & Chen, 1991; Farago & Mehra, 1993
- Use of bacteria to leach or to precipitate copper - Ostrowski & Sklodowska, 1993; Panchanadikar & Kar, 1993

Copper and plants -
- Algae, fungi and bryophytes - Calmano et al., 1992; Florence et al., 1992b; López & Carballeira, 1993; Lüderitz & Scholz, 1989; Rao & Gowrinathan, 1992; Rijstenbil & Poorvliet, 1992; Tolomio et al., 1990
- Native plants - Hopmans et al., 1993; Neite et al., 1991
- Domestic plants - Ahmadi et al., 1993; Browaldh, 1992; Folsom & Houck, 1991 (computer program to predict plant uptake); Gimenez et al., 1992; Gorlach & Gambus, 1991; Kubota et al., 1992; Mullins & Burmester, 1993; Qin et al., 1992; Taylor et al., 1993b; Thomson et al., 1993; Turski et al., 1990a; Tyksinski, 1987a; Wolters et al., 1992; Zhu & Alva, 1993d

Copper and animals -
- Invertebrate animals - Mitra et al., 1992a; Porta & Ronco, 1993; West et al., 1993a; Ying et al., 1992
- Vertebrate animals - Hickie et al., 1993; Kaviraj & Das, 1991
- Domestic animals - Aoyagi et al., 1993a; Bertechini & Hossain, 1993; Henry et al., 1993b
- Laboratory animals - Larsen & Sandström, 1992b
- Miscellaneous - Arena et al., 1993

Copper in food materials - Arcos et al., 1993; Gahlawat & Sehgal, 1993; Hurley & Lönnerdal, 1988; Vaquero et al., 1992

Copper and human nutrition - Brzozowska, 1991; Yoshida & Senda, 1993

Removal of copper from beverages - Wucherpfinnig, 1992a,b

III.3 ORGANIC COMPLEXING AGENTS

The biological availability of copper in the environment as well as its uptake, transport and use in organisms is affected by organic complexing agents. Recent references concerning these organics are provided in section I.7 (Interaction of copper with organics) in this review.

III.4 ADSORPTION AND DESORPTION

Particles and fibers can acquire and lose copper through sorption processes. There is competitive interaction between soluble complexing agents and particulate sorbing agents for ionic copper as well as the potential for uptake of some complexed copper species by sorption. The movement of particles, ranging from colloids to silts and clays, by rivers as well in estuaries and salt water provides an important mechanism for the distribution of metals, including copper (e.g. Ongley et al., 1992; Rees, 1991). Sorption processes can be beneficial in the isolation of metals from water (e.g. Barg et al., 1993; Das land Bandyopadhyay, 1992; Rigas et al., 1991) including drinking water and waste water (e.g. De Boodt, 1991). Copper-containing clay suspensions have been proposed as a mechanism for controlling snail intermediate hosts of schistosomes, the causative agent for schistosomiasis (Al-Sabri et al., 1993).

Recent references dealing with the range of sorption mechanisms and sorption/desorption processes include the following:

Organic particles including organisms and organic-containing synthetic agents

- Microorganisms .... Avery & Tobin, 1993; Falla & Block, 1993; Mayers & Beveridge, 1989
- Fungi and yeasts ....Miyoshi et al., 1992 (fungal chitosans); Sarishvili et al., 1992
- Mosses ....Mersch et al., 1993
- Algae........................ Chen et al., 1993c (alginate); Mokhtar et al., 1991 (alginate); Pascucci, 1993
- Plants .... Bryant et al., 1990 (sawdust); Low et al., 1993 (palm fibres); Said et al., 1993 (cellulose); Zhao et al., 1990 (Chinese tea)
- Chitin from crustaceans...Mokhtar et al., 1991
- Miscellaneous ....Monbouquette et al., 1993 (biomimetic metal-sorbing vesicles)

Soils and soil materials

- Soil adsorption ....Basta et al., 1993; Halen et al., 1991; Wang & Liu, 1991; Zhu & Alva, 1993b
- Clay-based materials....................Halen et al., 1991; Keizer & Bruggenwert, 1991; Micera et al., 1992
- Effect of organic material on soil sorption..................................Borah et al., 1992
- Humic substances and sorption ....Bunzl & Schimmack, 1991; Sekulic, 1990a,b, 1991

Materials in aquatic systems

- Effect of organics ....Wang, 1992
- Riverine particles .... Ruiz & Romero, 1992
- Estuarine systems .... George, 1993; Regnier et al., 1990
- Sediments... Chester, 1988; Young et al., 1992
- Miscellaneous ....Brinkman, 1993; Gutzman & Langford, 1993; Koch & Grupe, 1993

III.5 METAL-METAL INTERACTIONS WITH ORGANISMS

The uptake, metabolism and accumulation of copper by organisms can be affected by the action of other ions (e.g. Naylor, 1989 (Ph.D. Thesis); Pellegrini et al., 1993; Rhee and Thompson, 1992 (review of sorption kinetics in phytoplankton); Shuttleworth and Unz, 1993). Interactions may be synergistic or antagonistic (Rachlin and Grosso, 1993) and may be reflected in correlations among elements in biological materials (Moro et al., 1992). A number of variables must be accounted for in studies of the role of copper in ecological and physiological functions. For example, metal ions may compete for binding sites on proteins such as metallothionein (Witkowska et al., 1991) and a deficiency of essential trace elements (Fe, Cu, Zn) may increase the toxicity of trace elements (e.g. Cd, Pb, Hg) (Wu, 1992b). The concentrations and chemical forms of other ions will also vary in time and space, under control of their own set of environmental and biological processes (e.g., Metayer et al., 1992). The complexity of metal-metal interactions has important implications for bioassays and the toxicity testing of mixtures since multiple elements and compounds often co-occur in industrial and/or agricultural residues (Mullick and Konar, 1991, 1992; Sekkat et al., 1992). The addition of phosphorus to soil changes the chemical forms of ions, moving copper from less soluble to more soluble forms (Kaushik et al., 1993). Recent references that deal with metal-metal interactions include the following:

Copper-iron - Bazylinski et al., 1993; Blowey, 1992; Bolann and Ulvik, 1993; Elhardallou and Walker, 1992; Fields et al., 1993b; Gordon et al., 1993b; Greipsson, 1992; Hill, 1992; Kochian et al., 1993; Kolb et al., 1992a; Lan et al., 1992; Larsen and Sandström, 1992b; Lee et al., 1992; Li et al., 1993b; Lidon and Henriques, 1993a; Marzabadi and Jones, 1992; Newhouse et al., 1993; Quinn et al., 1993; Rogers, 1992; Schroth et al., 1993; Seliga, 1993; Shaw et al., 1992; Singh et al., 1992a; Sui et al., 1991b; Uehara et al., 1987, 1988, 1990a, 1991; Van Houwelingen et al., 1993; Yabuki et al., 1991; Yamagushi et al., 1991

Copper-cadmium - Kessels and Wensing, 1993; Gully and Mason, 1993; Kaji et al., 1992; Kuhnert et al., 1993; Mwangi and Alikhan, 1993; Rambeck et al., 1991; Turnau, 1990, 1991; Zaroogian et al., 1992

Copper-Manganese - Lidon and Henriques, 1993a

Copper-molybdenum - Arthington et al., 1993; Brem et al., 1992; Bremner, 1991a (Review); Chatterjee et al., 1992; Giroussi et al., 1993; Gooneratne and Christensen, 1991b; Haroun et al., 1992; Hernández-Pérez et al., 1992; Nass et al., 1993; Quiroz-Gutiérrez et al., 1992; Wang et al., 1992f;

Copper-nickel - Bagatto et al., 1993; Lee and Chang, 1991; Mwangi and Alikhan, 1993; Sachdev et al., 1993

Copper-silver - Martoja and Marcaillou, 1993

Copper-zinc - Abu-El-Zahab et al., 1991; Angelow and Yanchev, 1991; Arquitt et al., 1993; Bagatto et al., 1993; Brewer et al., 1993b; Briske-Anderson and Reeves, 1993; Dragnev et al., 1991; Gachot and Poujeol, 1992; Gartside and Glueck, 1993; Graham and Keen, 1992; Greger and Kautsky, 1992; Hermann et al., 1993b; Huang et al., 1991c; Jia et al., 1991; Kargin et al., 1992; Larsen and Sandström, 1992b; Lee et al., 1991a; Lee et al., 1993b; Martoja and Marcaillou, 1993; Menara et al., 1992; Peretz et al., 1993; Qian et al., 1993; Rao and Parry, 1991; Rijstenbil and Poortvliet, 1992; Steinebach and Wolterbeek, 1992a; Swinkels et al., 1993; Thomas et al., 1993; Turnlund et al., 1991; Van Houwelingen et al., 1993; Werman and Bhathena, 1992

Copper-lead - Kreuzer et al., 1991; Morawiec, 1991

Copper and other metals and metalloids - Adekalu and Heaton, 1992; Angelow and Yanchev, 1991; Batley et al., 1992; Bires et al., 1991a; Castro et al., 1992a; Cossa et al., 1992; Cowgill and Landenberger, 1992; Foster et al., 1993; La Ruche and Césarini, 1991; Olin et al., 1993; Prairie et al., 1993; Rader et al., 1991; Schmolke et al., 1992; Tarp et al., 1991; Wapnir et al., 1993; Yoshida et al., 1991; Hermann et al., 1993b

Calcium - Alva et al., 1993; Bjerselius et al., 1993; Gu et al., 1991b; Hermann et al., 1993b; Pellegrini et al., 1993; Qian et al., 1993; Tyksinski, 1987b; Yamaguchi, 1993; Yang and Roru, 1991

Miscellaneous - Abdelrahman and Kincaid, 1992; Allen et al., 1993; Ankley et al., 1993a; Chatterjee et al., 1992; Gill et al., 1992; Hendricksen et al., 1992; La Ruche and Césarini, 1991 Maciejewska, 1992; Nus et al., 1993; Navarro Pedreno et al., 1992; Qi et al., 1993; Rhoads et al., 1992; Thomson et al., 1993; Verma et al., 1993

IV - Uptake and accumulation of copper by organisms

The acquisition of copper by organisms, whether it is from the environment or from food, involves uptake and the mechanisms associated with uptake (e.g. Trif et al., 1992). The fate of metal once acquired, involves mechanisms associated with transport, storage and excretion. As a result, information on metal uptake and accumulation is of importance in a variety of topics. These include the assessment of copper requirements by plants and animals (e.g. Marchal et al., 1991), soil testing for available copper (e.g. Watanbe, 1992), stimulation of metal uptake (e.g. Ghosh and Bupp, 1992), the effect of metal-metal interactions on uptake (e.g. Adekalu and Heaton, 1992; Wapnir et al., 1993) and copper transport in healthy as well as diseased organisms (e.g. Harris, 1993; Houwen et al., 1993; Sorenson, 1992b). Understanding metal uptake and storage is also important when dealing with the impact and recovery of areas affected by anthropogenic metal (e.g. Punz and Sieghardt, 1993; Summers, 1992). Titles of some pertinent articles are provided in the bioaccumulation sections of the U.S. National Technical Information Service series (1993a,b). References dealing with uptake and accumulation are often of a regional nature (e.g. Penpkowiak and Szefer, 1992; Vakarenkol et al., 1992; Varanasi et al., 1989). They may also discuss the use of organisms to take up anthropogenic copper in effluents (e.g. Gadd, 1992; Mishra et al., 1991; Wong and So, 1993; Wong et al., 1993d). Since uptake occurs only if the metal is in a biological available chemical state, any reference series on uptake and accumulation must include appropriate references dealing with the chemical nature of organics which may regulate the biological availability of copper (e.g. Bremner, 1991a; Henry and Harrison, 1992; Linnik and Osadchaya, 1992).

References given below are organized with respect to particular groups of organisms, biological impact or metal bioavailability:

Metal uptake and accumulation in bacteria, fungi, algae, mosses and lichens

Reviews..Lepp, 1992

Copper complexing metabolites............................ Bérail et al., 1992; Cabral, 1992

Metal bioavailability..López & Carballeira, 1993

Bacteria... Avery & Tobin, 1993; Becker et al., 1992; Cabral, 1992; Cha & Cooksey, 1993; Cooksey, 1993; Falla & Block, 1993; Farago & Mehra, 1993; Fitch et al., 1993; Fowler, 1990; Pruess & Speidel, 1993; Ruddick, 1992 (bacterial depletion of copper from CCA-treated wood); Shuttleworth & Unz, 1993; Tubbing et al., 1993b; Yazgan et al., 1993; Wu, 1992a

Cyanobacteria (blue-green algae)..........................Dwivedi et al., 1992; Lüderitz & Scholz, 1989 (results indicate species specific pH optima for uptake)

Algae................. Barreiro et al., 1993; Bassi & Sharma, 1993a; Bérail et al., 1992; Chang & Sibley, 1993; Gowrinathan & Rao, 1991; Greger & Kautsky, 1992; Mahan & Holcombe, 1992; Pascucci, 1993; Ramelow et al., 1992a; Rhee & Thompson, 1992; Zafaralla & Mangaban, 1990; Zolotukhina & Gavrilenko, 1992; Vymazal, 1990; Zolotukhina et al., 1991, 1992

Mosses ....López & Carballeira, 1993; Wang et al., 1992c; Watkinson, 1992

Yeast and fungi............................ An et al., 1993b; Borella et al., 1991; Lin, 1991a (Ph.D. thesis); Matsumoto & Tokimoto, 1992; Purkayastha & Mitra, 1992; Rizzo et al., 1992; Sanglimsuwan et al., 1993; Sarishvili et al., 1992; Turnau & Kozlowska, 1991

Lichens..Sloof & Wolterbeek, 1993b

Metal uptake and accumulation in plants

Reviews...Kahle, 1993

Metal bioavailability in soils/water............Angelone et al., 1993; Chlopecka, 1993; Fagbenro & Agboola, 1993; Hogg et al., 1993; Jackson et al., 199, 1993; Kuiters & Mulder, 1993a,b; Larson et al., 1992; Reboredo, 1993
Mechanisms of uptake ....Castro & Cotorás, 1992a; Hamed et al., 1993; Yang & Kuboi, 1991; Yruela et al., 1993
Prediction of metal uptake .... Folsom & Houck, 1991
Aquatic plants (includes bog plants but not domestic plants such as rice)............... Farago & Mehra, 1992; Jackson & Kalff, 1993; Jackson et al., 1992, 1993; Mackun et al., 1993; Reboredo, 1993
Forest/woody habitat species (including domesticated varieties)............................ Lukaszewski et al., 1993; Novacek, 1987a,b, 1988; Rachwal et al., 1992
Domestic plants
Grains .... Bassi & Sharma, 1993b; du Preez & Bennie, 1992a,b; Kubota et al., 1992; Nogales et al., 1987; Padole, 1991; Turski et al., 1990a; Wojcieska et al., 1989
Rice .... Lidon & Henriques, 1993d; Mohapatra et al., 1993
Fodder plants (includes alfalfa)..Douka et al., 1993
Fruit plants.. Tagliavini et al., 1993
Food plants .... Heinen et al., 1991; Lee et al., 1991c; Kubota et al., 1992; Lisbâo et al., 1991; Mauk & Nooden, 1992; Mineev et al., 1991; Narwal et al., 1992; Ogunmoyela & Esan, 1990; Singh & Ram, 1992; Slipcevic et al., 1993; Tyksinski, 1987a; Welch et al., 1993
Other commercially important plants .... Hood et al., 1993; Mullins & Burmester, 1993
Miscellaneous plants .. Andrzejewska et al., 1990; Pan, 1991; Rao & Dubey, 1992; Ryczkowski & Reczynski, 1991; Sato et al., 1992; Svenson & Witte, 1992; Zhang et al., 1992f; Zhu & Alva, 1993d

Metal uptake and accumulation in invertebrate animals
Reviews.................................Viarengo & Nott, 1993 (mechanisms of heavy metal cation homeostasis in marine invertebrates)
Prediction of metal accumulation .... Amiard-Triquet et al., 1992; Blincoe, 1993b; Buckley, 1991b; Brisbin et al., 1990
Regional and ecosystem studies of metal accumulation.........Everaarts et al., 1993; Roth, 1992
Animal groups
Protozoa (single-celled animals)...................................... Abraham et al., 1992; Khadre & Butler, 1992
Sponges .... Richelle-Maurer et al., 1991
Nemertean worms ....McEvoy & Sundberg, 1993
Annelid worms (earthworms, polychaetes and leeches)......Kaviraj & Das, 1991; Schrader, 1992; Steenken et al., 1991
Molluscs - bivalves (including oysters and mussels).................. Amiard-Triquet et al., 1992; Bordin et al., 1992; Hameed & Raj, 1990; Han et al., 1993; Ikuta, 1991a,c; Ikuta & Morikawa, 1991; Metcalfe-Smith et al., 1992; Naylor, 1989 (Ph.D. thesis); Perdicaro, 1989
Molluscs - snails (gastropods) ....Ireland, 1993; Mason & Gully, 1993 (identification of sites of Cu accumulation and turnover by stable isotopic ratio analysis); Mitra & Choudhury, 1993b; Ying et al., 1993
Molluscs - other........................... Martoja & Marcaillou, 1993; Shibata, 1992b

Weight loss ....Lykken & Klevay, 1992
Physical exercise ....Ohno et al., 1993
Copper losses in burns...Berger et al., 1992b
Copper in granulomas and gallstones.................................. Henry et al., 1993a; Koshinaga et al., 1991
Neurological disorders .... Iwakawa et al., 1993
Cardiovascular diseases..Moat et al., 1993
Abnormal growth (cancer) ....Shiotani et al., 1993
Disorders of copper transport..Danks, 1993

Chemical factors involved with the transport and fate of copper
Reviews.. Ross, 1993
Carrier agents and processes....................................Dadfarnia & Shamsipur, 1992; Menger & Lee, 1993; Shimaoka et al., 1993; Stephan & Scholz, 1993 (nicotianamine, mediator of transport of iron and heavy metals in plants); Suzuki et al., 1992c
Metallothionein-like agents (and their genetic control)..................Bremner, 1991b; Evans et al., 1992b; Farrell et al., 1993; Freedman et al., 1993; Lee et al., 1994; Ringwood & Brouwer, 1993; Sakurai et al., 1993a; Takatera & Watanabe, 1993; Wlostowski, 1992
Ceruloplasmin...............Bertoni et al, 1991; Lee et al., 1993e; Livshits et al., 1992; McArdle & Spenser, 1993; Stern & Frieden, 1993; Yamada et al., 1993a
Secretion/excretion of copper ....Ballatori, 1991; Dijkstra et al., 1993

V - CHANGES OCCURRING IN COPPER AFTER INTRODUCTION INTO NATURAL ENVIRONMENTS

When copper is introduced into a natural environment, or from one type of environment to another, the metal can be exposed to different chemical conditions. This quite often leads to changes in metal speciation and changes in metal bioavailability. The amount of metal entering an environment and the chemical changes that occur are of importance in determining the fate of the metal as well as its biological impact. As a result, a number of studies have examined the flux of metals, including copper, as well as metal speciation (e.g. Report number 32 of the Joint Group of Experts on the Scientific Aspects of Marine Pollution (GESAMP)). Monitoring programs can also provide evidence of the level of anthropogenic input as well as some indication of the source of the metals. Wollast (1990), for example, comments that information from surveys of the Rhone river have provided evidence that "... trace metal concentrations in the Rhone are significantly lower than previous estimates and that although anthropogenic signals are present, the Rhone river is less polluted than expected". Zabel (1993) comments that diffuse sources of pollution have increased in importance with the strict controls on point source industrial discharges. Summary information on metal flux and the changes that occur in metal speciation can be found in a variety of recent references (e.g. Lääne & Wilhelms, 1993; North Sea Task Force, 1993; Prandle, 1992), including references concerned with water quality (e.g. Carbiener & Tremolieres, 1990; Davis, 1993). The role of specific groups of chemicals in effecting changes in the speciation of copper is also discussed in a number of recent references (e.g. McKnight, 1991; Simon et al., 1992). There has been application of this information to problems faced by man (e.g. de Lourdes da Silva Leal & de Luca Rebello Wagener, 1993; Gutzman and Langford, 1993; Lin et al., 1993b; Martin & McCutcheon, 1992) as well as the development of models to assist in the explanation of environmental conditions (e.g. Brinkman, 1993)

V.1 COPPER IN ESTUARIES

The introduction of riverine material into coastal ocean waters occurs in an estuary, an area of rapidly changing salinity and river flow conditions. Quite frequently, estuaries provide important harbours with elevated population densities and shipping traffic. Conditions in these areas can produce elevated levels of natural and anthropogenic metals. As a result, they are of concern from an environmental standpoint (e.g. Sung, 1991; Wong et al., 1993c). References deal with metal sources and speciation as well as impact and policy implications.

Reviews (includes pertinent references on coastal oceanic areas)....Adriano, 1992 (editor); Brügmann, 1993; Hoppema & de Baar, 1992; McMahon, 1990; Michaelis, 1991; Sadiq, 1992

Metal speciation and fate of metals in estuarine and coastal environments (includes modelling studies) .... Brekhovskikh et al., 1991; Buckley & Winter, 1992; George, 1993; Hanson et al., 1993; Kuijpers et al., 1993; Lapaquellerie et al., 1992; Lapp & Balzer, 1993; Li et al., 1992a,b; Martin et al., 1993; Paulson et al., 1993a; Real et al., 1993; Regnier et al., 1990; Shumilin et al., 1993; Sung, 1991; Wang et al., 1993c; Windom et al., 1989; Wong et al., 1992; Xu et al., 1992a; Zhang et al., 1992a

Effect and implications of urbanization..McCreary et al., 1992

Metal sources in estuaries (or to ocean from estuaries)...............Benninger & Wells, 1993; Davis et al., 1992; Dunn et al., 1992; French, 1990 (Ph.D. thesis); Liao et al., 1993; Regnier & Wollast, 1993; Shao & Wang, 1992; Trefry et al., 1992; Yeats, 1993

Variation in levels and nature of input........................... Flegal & Sañudo-Wilhelmy, 1993; French, 1993b; Nair & Balchand, 1992; Riso et al., 1993; Sung, 1991

Pollution-induced biological effect....................... Burgess et al., 1993c; Duer et al., 1993; Sfriso et al., 1992; Xu et al., 1992a

References dealing primarily with sediments in estuaries and coastal seas..........................
Bonnevie et al., 1993; Buckley & Winters, 1992; Burgess et al., 1993c; Hanson et al., 1993; Lapp & Balzer, 1993; Nair & Balchand, 1992; Real et al., 1993; Weis et al., 1993 (copper, chromium and arsenic in estuarine sediments adjacent to wood treated with chromated-copper-arsenate; metal concentration could be related to age of wood and poor water exchange); Ye et al., 1991; Zhan et al., 1992; Zhang et al., 1992a; Zöllmer & Irion, 1993

V.2 COPPER IN FRESHWATER ENVIRONMENTS

Changes in metal form and speciation occurring in freshwater can be caused by a number of physical, chemical and biological factors, particularly pH (e.g. Matschullat and Wyrobek, 1993). These relate to particulate and dissolved fractions of an organic or inorganic nature. Although a number of the recent references are process oriented, others deal with metal sources or provide values and details of metals in freshwater environments.

Reviews ....Adriano, 1992 (editor); Gerhardt, 1993; Krishnamurthy, 1992

Metal sources (includes within-water species changes producing sources or cycling of metal).. Calderoni & Mosello, 1990; Elsokkary, 1992; Gragnani & Torcini, 1990 (Antarctica - meltwater lakes, coastal waters, etc.); Hupp et al., 1993; Migon, 1993; Poppe & Moffett, 1993; Ramelow et al., 1992b; Rang & Schouten, 1988; Reczynska-Dutka, 1990a,b, 1991; Reynolds & Hamilton-Taylor, 1992; Rossi et al., 1992; Saeki & Okazaki, 1993; Zhang & Zhou, 1992

Humic substances and other copper-complexing organics..
Krishnamurthy, 1992; Linnik & Osadchaya, 1992; Oden et al., 1993; Zyczynska-Baloniak et al., 1991

Suspended particulate material .... Hellmann, 1992; Wilken et al., 1991

Sorption/desorption..Mayers & Beveridge, 1989; Young et al., 1992 (excellent discussion of the processes although without direct reference to copper)

Benthic sediments.....................................Arakel & Hongjun, 1992; Arbouille et al., 1989; Bradley, 1988; Cornwell & Kipphut, 1992; Förstner & Kersten, 1988; Howa & Vernet, 1989; Norton et al., 1992; Pardo et al., 1993; Puckett et al., 1993; Rowan & Kalff, 1993; Saeki et al., 1993b; Sanders et al., 1993; Span et al., 1992; ten Hulscher et al., 1992; Vermette et al., 1987; Williams, 1992b

Metal flux (including seasonal changes)...Bradley, 1988; Förstner & Kersten, 1988; Hellmann, 1992; Matschullat et al., 1992; Migon, 1993; Ongley et al., 1992; Reczynska-Dutka, 1990b; Sanders et al., 1993; Stabel et al., 1991; Strunk, 1992; ten Hulscher et al., 1992; Vaithiyanathan et al., 1992

Metal sinks... Hupp et al., 1993; Morgan et al., 1992 (use of hydrogen sulfide as an immobilizing agent for heavy metals in the restoration of groundwater quality following mining operations); Puckett et al., 1993; Stabel et al., 1991

Speciation and metal bioavailability ....Jackson et al., 1993

Models used to determine metal speciation or metal flux..
Rowan & Kalff, 1993; Yu et al., 1991 (vertical movement of several metals in a dimictic calcium-chloride-type salt lake in Antarctica)

Techniques other than models for estimating metal speciation and/or flux..........................
Luan et al., 1992; Pardo et al., 1993; Rauret et al., 1988

V.3 COPPER IN MARINE ENVIRONMENTS

Copper enters the marine environment primarily from riverine transport and aerosols. Anthropogenic as well as geothermal sources can also be included, although these tend to vary on a regional basis. Changes occurring after entry include those occuring during estuarine transport as well as processes occurring in the water column, the sediment-water interface and within the sediments (including any refluxing that occurs). Temporal and spatial variability occurs in metal speciation as a result of physical as well biological events (e.g. Elbaz-Poulichet et al., 1990).

Reviews ....Brügmann, 1993 (Environmental Review for the Baltic Sea); Chester, 1988; Fischer & Wartel, 1992 (Trace metals in the Marine Environment); Hoppema & de Baar, 1992 (Relations between North Sea and Atlantic Ocean); Sadiq, 1992(editor of Toxic Metal Chemistry in Marine Environments)

Sources of copper ....Basford et al., 1993; Brügmann et al., 1992; Cabioch, 1993; Chester, 1988; Gragnani & Torcini, 1990; Kersten et al., 1990; Lewis & Landing, 1992; Morley et al., 1990; Osuna López et al., 1986; Shao & Yang, 1991; Walkusz et al., 1993; Wollast, 1990; Zöllmer & Irion, 1993

Metal chemistry, flux and cycling (including variations in concentrations).......................... Brügmann et al., 1992; Ciceri et al., 1992; Elbaz-Poulichet et al., 1990; Fowler, 1990; Hudson & Morel, 1993; Hydes & Kremling, 1993; Jackson et al., 1994 (a mass-balance analysis of trace metals in two weedbeds); Prabhakaramurty & Satyanarayana, 1990; Remoudaki et al., 1991; Schönfeld et al., 1990; Takematsu et al., 1993 (sediment metal distribution as predicted by a simulation model); Tambiyev et al., 1992; Tappin et al., 1993; Tsunogai et al., 1982, 1990; Wang et al., 1992e; Yamamoto, 1992

Benthic sediments .... Basford et al., 1993; Gerringa et al., 1991; Osuna López et al., 1986; Takematsu et al., 1993 (sediment metal distribution as predicted by a simulation model); Walkusz et al., 1992; Zöllmer & Irion, 1993

V.4 COPPER IN TERRESTRIAL ENVIRONMENTS, PARTICULARLY SOILS

Copper occurs in soils in varying amounts as a result of the chemical nature of the soil parent material and diagenetic processes which have occurred since its formation (e.g. Plichta and Kuczynska, 1991; Zierdt, 1990). The metal can be associated with the inorganic or organic fractions of soil material, being found within the matrix or sorbed to inorganic particles or complexed by either inorganic or organic molecules within the soil. Cultivation, fertilization and other soil management practices affect the chemical associations of copper in soils, including those that affect the biological availability of the metal to economically important plants. The following recent references provide information on the sources of copper to terrestrial environments, the disposition of the metal and some of the changes that can occur in metal speciation.

Sources of copper in soils (includes anthropogenic sources)....................Lee et al., 1991b; Wannemacher, 1991

- Pesticides....................................Neary et al., 1993; Schauder & Auerswald, 1992
- Sewage sludge.................... Benes, 1991; Chino et al., 1992; Juste & Mench, 1992
- Mining and electroplating ...... Chen, 1992b; Di Gregorio & Massoli-Novelli, 1992; Hyun & Yoo, 1991; Macías et al., 1992; Rachwal et al., 1990; Tai, 1991
- Miscellaneous... Minoranskij & Wojciechowski, 1991

Seasonal and spatial variability in soil metal concentrations........Obukhov & Popova, 1993

Chemistry and flux of copper in soils (includes trace element budgets and chemistry of copper in soils containing anthropogenic copper).. Benes & Benesova, 1992, 1993; Biddappa et al., 1991; Bowell & Ansah, 1993; Chino et al., 1992; Di Gregorio & Massoli-Novelli, 1992; Harmsen, 1992; Hyun & Yoo, 1991; Juste & Mench, 1992; Keller et al., 1992a; Komisarek et al., 1990; Kratz, 1991b; McGrath & Cegarra, 1992; Menon et al., 1993; Neary et al., 1993; Parmar & Gupta, 1992; Plichta et al., 1991; Protz et al., 1993; Raghupathi & Vasuki, 1991, 1992; Sekulic, 1990b; 1991; Selim et al., 1990 (modeling the transport of heavy metals in soils); Turski et al., 1990b; Varshal et al., 1992; Versfeld & Donald, 1991; Wang & Liu, 1991

Impacts of harvesting on soil copper levels..Hopmans et al., 1993

V.5 AEROSOL COPPER

Airborne copper is an important source of metal, particularly in regions near industrialized areas (e.g. Haaygarth and Jones, 1992). Preston (1992) comments on the importance of the atmospheric flux of pollutants to the oceans. Rao and Dubey (1992) discuss the accumulation of aerosol metals by tropical plants growing in an industrial area, noting differences in the ability of the plants to scavenge the metals. The biological effect of aerosol copper, by itself, is difficult to identify because of the interacting effects of other aerosol agents, like acids and other metals (e.g. Vesely et al., 1993).

Reviews ....Haygarth & Jones, 1992; Preston, 1992

Sources of atmospheric copper..............Romo-Kröger & Llona, 1993; Vernon et al., 1992

Estimates of atmospheric inputs to particular regions.............................Guieu et al., 1990 (Gulf of Lions); Holsen et al., 1993 (Lake Michigan); Infante et al., 1989 (Ponce, Puerto Rico); Lim, 1991 (Ph.D. thesis on trace metals in North Atlantic precipitation); Migon, 1993 (Ligurian Sea); Ottley & Harrison, 1993 (North Sea); Remoudaki et al., 1991 (western Mediterranean Sea); Suttie & Wolff, 1992 (seasonal input of 4 ng kg^{-1} copper to Antarctic snow)

Spatial and temporal variability of deposition...................................Gailey & Lloyd, 1993; Injuk et al., 1992; Irvine et al., 1989

Solubility (and factors controlling the solubility) of atmospheric aerosol copper................ Chester et al., 1993; Giusti et al., 1993; Gu et al., 1991a; Hamilton-Taylor et al., 1993

VI - COPPER CONCENTRATIONS IN THE ENVIRONMENT

Copper levels in natural environments continue to be of interest from the standpoint of metal adequacy and excess. Reviews include discussions of conditions and metal concentrations in estuaries and bays (e.g. Dalziel et al., 1993; Michaelis, 1991; Phillips et al., 1992) as well as methods of collection and measurement of copper in environmental samples (e.g. Senesi, 1992; Yeats and Brügmann, 1990). Ciceri et al. (1993), for example, describe a benthic instrumentation and monitoring system that allows estimations of the benthic fluxes of particulate metal. Guidelines for the determination of selected trace metals in aerosols and wet precipitation are provided in a publication of the United Nations Environment Programme (1988) and standards and reference materials for marine science are given in a 1993 Unesco publication, by the Intergovernmental Oceanographic Commission.

Metal concentrations are subject to variability with both time and space while measured values may be subject to error from artifacts associated with sample collection, preparation and analysis (e.g. Houba et al., 1993; Schults et al., 1992; Thompson and Maguire, 1993). Sample collection sites must be selected carefully (Symader, 1993) while quality of collection and sample handling is critical to accuracy of the metal values (e.g. Davis, 1992; Valette-Silver, 1992). When properly done, environmental metal levels can be used as predictors (e.g. Rowan and Kalff, 1993) as well as indicators of existing conditions and changes over time and space. This often involves statistical treatment to better permit predictions or site assessments (e.g. Lutwick and Krzanowski, 1992).

Recent references deal with sample treatment as well as methods of metal analysis:

Metal extraction from soil and water samples
- Soil extraction techniques and evaluations.............Alt & Peters, 1992; Alva, 1992; Baydina, 1993; Clifford et al., 1993; de Kreij et al., 1993; Gerzabek, 1993; Haddad & Evans, 1993; Rechcigl et al., 1992; Reed et al., 1993; Sapek & Sapek, 1992; Shan & Chen, 1993; Voelkel & Szymanowski, 1993; Walworth et al., 1992; Zhu & Alva, 1993a
- Concentrating mechanisms for copper in water and sediments
  - Freshwater (including drinking water)................................Bekova et al., 1993; Burba & Blödorn, 1992; Burba et al., 1992a; Chambaz & Haerdi, 1992a; Hsieh & Liu, 1993; Kastelan-Macan et al., 1992 (separation of "dissolved" humic acids from natural waters); Mahan & Holcombe, 1992; Rigas et al., 1991; Sarzanini & Mentasti, 1991 (review of metal ion preconcentration techniques, primarily in freshwater and saltwater); Shamsipur & Alizadeh, 1992; Verweij, 1993
  - Saltwater ....Baffi et al., 1993; Barg et al., 1993; Blain et al., 1993; Burba & Blödorn, 1992; Burba et al., 1992a; Liu & Huang, 1992, 1993; Mahan & Holcombe, 1992; Rao & Chatt, 1993; Sarzanini & Mentasti, 1991
  - Sediments ....Bendell Young et al., 1992; Chambaz & Haerdi, 1992a (interstitial water in sediments); López-Sánchez et al., 1993; Wallmann et al., 1993
  - Miscellaneous ....Bhowal et al., 1993 (UV-photolytic decomposition)

Recent references dealing with analytical techniques for environmental samples include:
- Colourimetric and flouorescent techniques.......................... Perez-Ruiz et al., 1992
- Atomic absorption spectrometry..............................Azeredo et al., 1993; Farah & Sneddon, 1993; Kojima et al., 1988; Li et al., 1991b; Naghmush et al., 1992; Soylak et al., 1993; United Nations Environment Programme, 1985
- Electrochemical techniques..................... Agraz et al., 1993; Beinrohr et al., 1993; Belli & Zirino, 1993; Díaz-Cruz et al., 1993; Esteban et al., 1992; Fukushima et al., 1992;

Ge et al., 1992; Horváth et al., 1992; Iyer & Sarin, 1992; Jagner et al., 1993; Kravtsov, 1992; Martinotti et al., 1992; Navrátilová & Kula, 1993; Neshkova, 1993; Ostapczuk, 1993; Sánchez-Pedreño et al., 1992; Scarano & Bramanti, 1993; Town & Powell, 1993; Ugo et al., 1993; van den Berg, 1992; Varney & Chevalet, 1993; Wang et al., 1992c; Zhao et al., 1992a

Inductively coupled and other plasma sources.........................Horváth et al., 1992; Huggins & Henion, 1993; Taylor et al., 1992 (ICPMS use for quantitative measurements of trace elements (not copper) in specific, submicrometer size-fraction particulates); Wills et al., 1993; Yamasaki & Tsumura, 1992; Yu et al., 1991b

X-Ray spectrometry....................................Haarich et al., 1993; Lau & Ho, 1993; Pepelnik et al., 1993; Prange et al., 1993; Schmidt et al., 1993

High performance liquid chromatography (HPLC)... Comber, 1993; Khuhawar & Soomro, 1992; Yamada et al., 1992b; Yasui et al., 1992

Miscellaneous.....................................Schmidt & Bahadir, 1993 (determination of arsenic in the presence of high copper concentrations); Segebade et al., 1993 (photon activation); Thuemmel et al., 1991 (photon activation)

VII - COPPER CONCENTRATIONS IN ORGANISMS AND FOOD

The concentration of copper, and other essential elements, in organisms is important when considering nutrient intake by humans (e.g. Wang et al., 1993a; Wolf, 1991), by domestic animals (e.g. Monkiewicz et al., 1991) and uptake by domestic plants. It is also important in evaluating potential harm from organisms that may contain high levels of heavy metals (e.g. Vetter, 1993). The U.S. National Technical Information Service (1993a,b) provides a list of some of the refernces dealing with heavy metal concentrations in freshwater and marine communities. Discussions of comparative studies and Standard Reference Materials that have recently been published include:

Comparisons of measurements....................... Arnaud et al., 1993 - multilaboratory comparison of serum copper measurements; Cortes Toro et al., 1993 - comparison of hair and body burden metal levels

Reference materials

General .... Intergovernmental Oceanographic Commission, 1993 - standards and reference materials for marine science

New materials .... Kucera et al., 1993 - apple and peach leaves (see also Kucera & Soukal, 1993a,b); Novozamsky et al., 1993 - cabbage and carnation; Quevauviller et al., 1992 - cod muscle; Quevauviller et al., 1993 - freshwater plankton; Zeisler et al., 1993 - cabbage

Reliability of reference materials.................... Okamoto, 1992 - human reference materials; Wyttenbach et al., 1993 - spruce needles

Miscellaneous .... Hancock et al., 1993 (use of reference data to separate native copper and European trade copper in archaeological copper and brass from northeastern Ontario, Canada); Xu et al., 1992b - general

Besides the recent references that deal with the use of specific techniques for preservation and analysis, several provide new or revised methods for determining copper levels in organisms and food materials (e.g. Barbera et al., 1991; Roos et al., 1992; Taskina, 1991; Valkovic et al., 1993). The following references deal with the treatment of biological material prior to analysis:

Preparation of biological materials for analysis............................ Baranowska et al., 1992; Fleurence & Le Coeur, 1993; Green & Mathias, 1993; Grüner et al., 1992; Günther et al., 1993; Ipach, 1992; Krushevska et al., 1993; Kupila-Rantala et al., 1993; Lajunen et al., 1992; Matusiewicz et al., 1991; Niazi et al., 1993; Nomata et al., 1993; Puri et al., 1991; Schramel et al., 1993; Skurikhin, 1993a; Soto-Ferreiro & Bermejo-Barrera, 1993; Takiyama & Ishii, 1992; Zhang, 1991b; Zimna, 1991; Zou & Cao, 1992

Variability occurs in tissue metal concentrations as a result of natural conditions as well as artifacts. References that address variability are important to an understanding of what tissue metal concentrations really mean. This is well discussed in an article by Maynard (1990) entitled "Environmental tests: Are they valid?" Recent references dealing with this aspect of organism copper concentrations include:

Variability as a result of natural conditions.............. Ando et al., 1991; Bartos et al. (1991a) and Ikuta (1991c); Nolan, 1991

Artifacts .... Robinson et al., 1993; Shibata et al., 1992a; Sturaro et al., 1993a; Villalba et al., 1993; Worley, 1993; Yoshino et al., 1993

Comparison of blood serum values in laboratory-reared fish with those in native fish .... Hunn et al., 1992

Limit of determination characteristics to minimize the effects of sample size and variability .... Skurikhin, 1993b

Correlations between metal levels in different plant tissues....................... Bartos & Farkas, 1992

Recent references dealing with analytical techniques for biological tissues (including human tissues) include:

Colourimetric techniques .... Cyganski & Krystek, 1992; Deng et al., 1992; Huang et al., 1991b; Lai & Chen, 1992; Ohno et al., 1992b; Pettitt & Brown, 1991; Rizk et al., 1992; Steenkamp & Coetzee, 1993; Umezawa & Akyoshi, 1993a,b; Zeng, 1992; Zhang et al., 1992d,e; Zhong & Tian, 1992

Atomic absorption spectrometry .... Alvarado et al., 1991; Atsuya et al., 1993; Berndt et al., 1993; Chung & Tsai, 1992; Farah & Sneddon, 1993; Garcia Mateo & Calatayud, 1993; Jaffe et al., 1992; Kojima et al., 1992; Liu et al., 1992; Luterotti et al., 1992; Netzer & Bandion, 1992; Pan & Wang, 1991; Su et al., 1992; Viñas et al., 1993; Wang & Demshar, 1993; Xu et al., 1992b; Xue, 1991

Electrochemical techniques....................... Fogg et al., 1993; Kobon & Nihei, 1992 Lyle & Yassin, 1993; Mannino et al., 1991; Michalowski & Trojanowicz, 1993; Mirzadeh et al., 1993; Reinecke et al., 1992; Sánchez-Pedreño et al., 1992; Zhang, 1991a

Inductively coupled and other plasma sources........................ Alimonti et al., 1989; Anderson et al., 1992; Asp & Lund, 1992; Caroli et al., 1992; Erwen et al., 1992; Fuge et al., 1993; Gélinas et al., 1992; Goto et al., 1992; Krusheva et al., 1993; Lin et al., 1991b; López-Artíguez et al., 1993; Sasaki et al., 1989; Shiraishi & McInroy, 1991; Simko et al., 1992; Sun et al., 1992; Thompson et al., 1991; Ward et al., 1992; Yoshinaga et al., 1993; Zhang et al., 1991d

Neutron activation........ Garg et al., 1993; Kucera & Soukal, 1993a,b; Yates, 1992

X-Ray fluorescence................................... Bao & Shen, 1992; Calliari et al., 1993; Custo et al., 1992; Frank et al., 1992b; Homma & Shimojo, 1992; Homma et al., 1992a; Li et al., 1991a; Yao et al., 1993; Zhang et al., 1991b

PIXE .... Glass et al., 1993; Katayama et al., 1993; Kupila-Rantala et al., 1993; Maenhaut et al., 1993; Nishide et al., 1993; Ojo et al., 1993; Protz et al., 1993; Samudralwar & Robertson, 1993; Tomita et al., 1993; Wu et al., 1993; Yao et al., 1993

MicroprobeBoscher-Barre & Trocellier, 1993; Boscher-Barre et al., 1992; Elliott & Grime, 1993;
Iida & Noma, 1993; Pallon et al., 1993; Staples et al., 1992; Watkinson & Watt, 1992

Miscellaneous .... Chambaz & Haerdi, 1992b; Kitagawa & Katoh, 1992 (atomic emission spectrometry); Li & Zhang, 1992 (catalytic fluorimetric determination of trace copper); Nagaosa & Bond, 1992 (HPLC plus electrochemical and spectrophotometric detection for metals in serum); Sturaro et al., 1993b (dynamic ion-exchange chromatography use with atomic absorption spectrometry and XRF)