

# Safety guidelines for copper in water<sup>1,2</sup>

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**ABSTRACT** It is important for public health authorities to set a scientifically sound guideline value for the safe ingestion of copper in drinking water. To date, the principal health-based guideline values have been set by the US Environmental Protection Agency (1.3 mg Cu/L) and the World Health Organization (2.0 mg Cu/L). However, close examination of the data and assumptions used in the derivation of these values reveals a paucity of scientifically defensible information. Several international groups are now reviewing this issue, and others have begun epidemiologic studies that may provide useful copper exposure and toxicity data. Investigations of acute copper toxicity in human populations are most likely to affect future revisions of the guideline value for copper in drinking water. *Am J Clin Nutr* 1998(suppl);67:1098S–1102S.

**KEY WORDS** Copper, guideline value, acute copper toxicity, drinking water, humans

## INTRODUCTION

Drinking water is potentially a major source of copper exposure because of the widespread use of copper pipes in household plumbing. Depending on the characteristics of the water (particularly pH), copper can leach into the water and subsequently be ingested. Under circumstances of low dietary copper intake, such leached copper may be an important dietary source, but generally one is concerned with the acute and chronic effects of overexposure to copper in drinking water.

Various attempts have been made to determine a safe concentration of copper in potable water. This article examines safety guidelines developed in several countries and provides historical perspectives of those guidelines. In addition, some recent copper guideline reviews and proposals are discussed, followed by an outline of current research activities that are attempting to more clearly delineate the threshold for toxicity of copper in water.

## GUIDELINES IN VARIOUS COUNTRIES

The health-based guideline values for copper in drinking water from several countries are shown in **Table 1**. In addition, aesthetics-based guidelines are in place in most countries; generally, the aesthetics guideline is the concentration of 1.0 mg/L proposed by the World Health Organization (WHO) and the US Environmental Protection Agency (EPA) (1–3). However, since

1993 the WHO has adopted a health-based value of 2.0 mg/L (discussed below), although it is apparent (after having contacted health authorities in several countries) that the 1.0-mg/L value is still the principal regulatory guideline in many countries. This aesthetics guideline is based on consideration of taste and staining of hand basins, bathtubs, and sinks. The taste threshold for copper is 1–5 mg/L (4, 5), the value apparently increasing with decreasing purity of the water (4).

In the main, the health-based values are guidelines only; in the United States, however, the health-based value has been mandated by legislation and is therefore an enforceable regulation, coming into play when copper in tap water that has been standing overnight exceeds 1.3 mg/L in >5% of samples (6). A health alert at 3 mg/L was proposed in South Australia (7); short-term excesses are predicted to carry a fair risk of acute symptoms (although this or any other guideline does not take into account the notion of acclimatization to high concentrations of copper in drinking water).

## Historical perspectives on copper guideline development

In prefacing this section, two points are made. First, the utilization of scientific information is the linchpin of guideline development. As will be seen, copper guidelines were originally devised from knowledge of aesthetic effects, but then observations of human toxicity response to ingested copper were brought to bear on the setting of guidelines. This section also highlights some of the problems that have beset the establishment of safety guidelines for copper in water. Second, the US EPA and the WHO are the principal groups that have been involved in developing copper guidelines. This section examines their approaches.

## US Environmental Protection Agency

Before the establishment of the US EPA in 1970, the US Public Health Service had set various guidelines for copper in drinking water over a time span of almost 40 y: 0.2 mg/L in 1925, 3.0 mg/L in 1942, and finally 1.0 mg/L in 1962 on the basis of taste complaints (3, 8). Then the US EPA Office of Drinking Water,

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**TABLE 1**  
Guideline values for copper in drinking water<sup>1</sup>

|                            | Guideline<br>mg/L |
|----------------------------|-------------------|
| Health-based guideline     |                   |
| US EPA                     | 1.3               |
| Australia                  | 2.0               |
| WHO                        | 2.0               |
| Aesthetics-based guideline |                   |
| WHO                        | 1.0               |
| European Commission        | 3.0               |
| Australia                  | 1.0               |
| US EPA                     | 1.0               |

<sup>1</sup> EPA, Environmental Protection Agency; WHO, World Health Organization. Aesthetics-based guideline is based on taste and staining of hand basins, bathtubs, and sinks.

after a review of the scientific literature on copper ingestion—both accidental (leached copper in water and beverages) and intended (suicide attempts with copper sulfate—decided to use information from a case study reported by John Wyllie in 1957. His report, “Copper Poisoning at a Cocktail Party” is reproduced in full below [(9); Copyright APHA; reprinted with permission from the American Public Health Association, Washington, DC].

An outbreak of food poisoning occurred following a cocktail party in the nurses’ quarters of a Military Hospital on August 12, 1954. The occasion was a private party given in honor of one of the nursing sisters who was leaving the unit. A cocktail consisted of: rye whisky—10 oz; fresh lemon juice—4 oz; egg white—1 teaspoonful; sugar melted—5 oz; water—6 oz; chipped ice to make—1 qt. It was prepared at 3 p.m. and placed in a refrigerator. Two cocktail shakers, each containing a quart, were removed at 5 p.m. and taken to the nurses’ lounge where about one quart was consumed. Within one-half to one hour following the consumption of the cocktails, nausea, vomiting and diarrhea ensued. Of the 15 nursing sisters, only five were without symptoms and fit for duty next day; the others felt weak, experienced abdominal cramps, dizziness, and headache.

In one cocktail shaker there still remained about a half fluid ounce of a pale green solution which gave positive chemical tests for copper. The interior of the shaker had a brown coating which contrasted sharply with the silvery coating of the cap. The evidence was suggestive of the original inner plating having become worn off through frequent use and cleaning during several years. A repeat trial of the cocktail was used to carry out extensive chemical tests for other metals and to determine quantitatively the copper content in one fluid ounce of the cocktail. Three of the participants consumed one-half glass of the cocktail, or three-quarters fluid ounces containing 5.3 milligrams of copper; five drank one glass, thus ingesting 10.65 milligrams of copper; four had two glasses or 21.3 milligrams of copper; and one had three glasses or 32 milligrams of copper. These amounts of copper are believed to have given rise to the symptoms of chemical food poisoning precipitated by the ingestion of alcohol on an empty stomach.

It is useful to summarize this study here to show how an important regulatory decision can rest on thin ice and to clarify the details of this report which, in some circles, seem to have been misconstrued, as can happen with old, almost folkloric, studies. One evening

at a military hospital in 1954 (presumably somewhere in Canada because Wyllie reported from Queen’s University Medical School in Kingston, Ontario), a group of nurses held a private party in honor of a departing nursing sister. Some of these nurses consumed a whisky cocktail that had been prepared in copper-containing shakers, and within 0.5–1 h experienced symptoms typical of acute copper intoxication (nausea, vomiting, and diarrhea). Wyllie then explains: “Of the 15 nursing sisters, only five were without symptoms and fit for duty next day: the others felt weak, experienced abdominal cramps, dizziness, and headache.” The cocktail (also known as a whisky sour) contained fresh lemon juice, melted sugar, water, chipped ice, and rye whisky in the volume ratio of 1:1.25:1.5:1.75:2.5, together with one teaspoon of egg white. A remake of this acidic mixture was shown to leach copper from the shakers, and with information from the nurses, Wyllie estimated how much copper each had consumed. He reported that three nurses ingested 5.3 mg (in 21 mL), five ingested 10.65 mg, four ingested 21.3 mg, and one ingested 32 mg Cu (9). Thus, 13 of the 15 nurses consumed the copper-cocktail, suggesting that of the 5 of 15 without symptoms, 3 had consumed some cocktail.

We are not told how much these three consumed, yet it is an important detail. If they were the same three nurses who consumed 5.3 mg Cu, then this amount could serve as the no-observed-adverse-effect level (NOAEL). However, US EPA regulatory scientists decided to use this figure as a lowest observed-adverse-effect level (LOAEL). The usual procedure is to then divide this figure by some factor (termed variously as the safety or uncertainty factor) to permit a margin of safety and, in the case of a LOAEL, to account for the fact that one is dealing with a response level and that the NOAEL is unknown. Commonly, no factor is used when a clear NOAEL has been established in a human study and a factor of 10 is used with a LOAEL. The US EPA used an uncertainty factor of 2 and then divided again by an assumed 2 L for daily water consumption, resulting in the guideline value of 1.3 mg/L (6). The reasons for the use of the uncertainty factor of 2 were that 1) the effect noted was local gastrointestinal irritation and was not permanent, 2) 5.3 mg was the lowest value found in the literature, 3) copper is an essential element, and 4) copper absorption is homeostatically controlled and the element tends not to accumulate in the body (10).

Recent commentaries have remarked on the approach taken by the US EPA (11–15). Although one can debate the use of nonempirically based uncertainty or safety factors, and the use of total copper intake compared with copper concentration (16), the principal concern with the above approach lies in the ambiguity and brevity of the Wyllie study. Key unanswered questions from Wyllie’s report are listed in **Table 2**; it is clear that this study has limited scientific and regulatory usefulness. Unfortunately, further details of the case study do not exist: no records of the event could be located at Queen’s University Medical School and John Wyllie died in 1971 (AF Clark and JC Wyllie, personal communication, 1995). Because the US EPA guideline for copper has been mandated by the US Congress, it may be an arduous task to institute any change. It will not be sufficient to merely point out deficiencies in the derivation of the guideline; good research is required to improve our understanding of the threshold of copper’s acute toxicity.

### World Health Organization

The only health-based guideline value for copper proposed by the WHO is 2.0 mg/L (17). As explained by Mercier (18), Director of the International Programme on Chemical Safety, this provisional value was derived in the following manner:

$$\begin{aligned}
 \text{Guideline value} &= (\text{tolerable daily intake} \times \text{body weight} \times \\
 &\quad \text{percentage intake from water}) / \\
 &\quad \text{adult daily water consumption} \quad (1) \\
 &= 0.5 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{d}^{-1} \times 60 \text{ kg} \times 10\% / (2 \text{ L/d}) \\
 &= 1.5 \text{ mg/L} \\
 &= 2 \text{ mg/L (rounded up)}
 \end{aligned}$$

For average adult body weight and daily water ingestion, the WHO uses default values of 60 kg and 2 L. They also work with a figure of 10% for the proportion of copper intake attributable to water (17). In reality, there would be considerable variation in these figures for individuals, but the default values chosen for derivation of the guideline are considered sufficiently conservative. The tolerable daily intake is defined as an estimate of the amount of a substance in food or drinking water, expressed on a body weight basis, that can be ingested daily over a lifetime without an appreciable health risk (17).

The 1993 WHO volume *Guidelines for drinking-water quality* (17) states, "Acute gastric irritation may be observed in some individuals at concentrations in drinking-water above 3 mg/litre. In adults with hepatolenticular degeneration, the copper regulatory mechanism is defective, and long-term ingestion can give rise to liver cirrhosis." Adult hepatic problems, which relate to the rare Wilson disease and which are dealt with in other articles in this supplement, generally do not affect guideline development for copper in drinking water. The former problem of acute toxicity also is only mentioned and, unlike in the US EPA approach, is not considered in the WHO development of a copper safety guideline.

Another issue addressed by this WHO volume is as follows: "Copper metabolism in infants, unlike that in adults, is not well developed, and the liver of the newborn infant contains 90% of the body burden, with much higher levels than in adults. Since 1984, there has been some concern regarding the possible involvement of copper from drinking-water in early childhood liver cirrhosis in bottle-fed infants, although this has not been confirmed" (17). After presenting the provisional 2-mg/L guideline value, the text goes on to say, "...a concentration of 2 mg/litre should also contain a sufficient margin of safety for bottle-fed infants, because their copper intake from other sources is usually low" (17).

It turns out that these concerns were largely the result of a

**TABLE 2**

Unanswered questions from John Wyllie's 1957 report of copper poisoning at a cocktail party<sup>1</sup>

|    |   |
|----|---|
| 1. | Did the alcohol and the nurses' fasted states exacerbate the acute effects of copper? (2.6–16 mL of ethanol was consumed, assuming 40% ethanol in rye whisky) |
| 2. | Did the three nurses who ingested the cocktail but were without symptoms the next day have acute symptoms at the party?                                       |
| 3. | Did the remaining two nurses who presumably drank no cocktail experience any health problems at the time of the party?  |
| 4. | Why did more than 2 y elapse between the incident and its reporting? Did this bias recall?  |
| 5. | What were the details of the "repeat trial of the cocktail" and the "extensive chemical tests for other metals"?  |

<sup>1</sup> From reference 9.

finding in Germany of clusters of supposed copper-induced liver pathologies in children in a region where well-water with a low pH passed through copper pipes and was then consumed (19, 20). Partly because of these concerns, the WHO working group that had reviewed the copper literature recommended a guideline value of no more than 1.5 mg/L. This figure was then rounded up to 2 mg/L within the WHO system to reflect the uncertainty in the data and assumptions (18). Although such rounding to one significant figure seems minor, it may be important in view of copper's narrow safety margin (20). [The clustering pattern of the above cases suggests the existence of a factor or factors in addition to copper and neonatal sensitivity. One possibility may be a genetic disorder similar to that which underlies endemic Tyrolean infantile cirrhosis (21).]

The actual derivation of the WHO guideline for copper of 2 mg/L has come into question because of several confusing ingredients, including apparent reliance on a 1972 classified study in dogs, a perpetuated transcription error between WHO documents, and uncertainty in the origin of the tolerable daily intake; these issues have been discussed at length (11, 12, 15). Regarding the study in dogs—since declassified (22)—it is now clear that the no-effect level (itself debatable) referred to by the WHO was in fact never used in the guideline equation but was seen as supporting the assumed human tolerable daily intake for copper set by the Joint FAO/WHO Expert Committee on Food Additives (11, 12, 23). Meanwhile, the tolerable daily intake of 0.5 mg/kg was proposed on the suggestion that 10 times the normal daily intake of copper, ie, 10 times 2–3 mg/d, would not elicit any health problems (23–26). The National Institute of Public Health and Environmental Protection in Holland has recommended a value of 0.17 mg · kg<sup>-1</sup> · d<sup>-1</sup> as the maximum intake of copper for lifetime exposure, which is based on the conclusion that "the total dietary intake of copper for adults will not easily exceed 10 mg" (27). This area needs review and consideration of more recent dietary information from a range of populations. Such information will also allow critical evaluation of WHO's use of the default 10% of total copper intake attributable to water; for average total intakes of, say, 3 mg Cu, this proportion is well exceeded by water concentrations ≥0.3 mg/L.

## RECENT REVIEWS AND PROPOSALS

### European Commission

Some water reticulation systems in Europe comprise lead piping and consideration is being given as to whether copper provides a safe alternative. The Scientific Advisory Committee of the Commission of the European Communities recently assessed the evidence for the toxicity of copper in drinking water. This included examination of the WHO's guideline development and of a range of animal and human studies. The main conclusions of this committee were that 1) animal data are insufficient, 2) human experience suggests that 1–2 mg Cu/L is acceptable, and 3) the proposed 2 mg/L in the draft of the European Commission drinking water directive should be retained (28).

### International Programme on Chemical Safety and Australia's National Research Centre for Environmental Toxicology

The WHO's International Programme on Chemical Safety is scheduled to produce an environmental health criteria document

on copper as a result of a meeting of a copper task force held in June 1996 in Brisbane, Australia. This document will contain relevant information on environmental exposures to copper and will summarize knowledge on copper metabolism, essentiality, deficiency, and toxicity. Before this meeting, Australia's National Research Centre for Environmental Toxicology in Brisbane hosted the meeting "International Workshop on Copper." Together, these forums provided significant focus to the actual and required data pertaining to copper toxicology and will make important contributions to the process of water quality guideline review.

#### Sidhu, Nash, and McBride

Sidhu et al (14) in the United States proposed a guideline for copper in water of 0.3 mg/L. These workers suggested that the US EPA guideline of 1.3 mg/L is not sufficiently protective of health, especially in children. Working with the 1957 Wyllie study used by the US EPA (9), these authors began with the lowest amount reportedly ingested by the nurses, 5.3 mg Cu, and then derived a reference dose by assuming an average body weight for women of 60 kg (thus,  $0.0883 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$ ), applied an uncertainty factor of 10 on the assumption that 5.3 mg is a LOAEL, and finally calculated a guideline value for a 70-kg adult consuming 2 L water/d (14). Their figure of 0.3 mg/L is certain to initiate some enthusiastic debate because compliance will be difficult in many reticulation systems. Scientifically, there has been debate over the approach used in the development of this guideline, with the principal concern surrounding use of the dubious data in the Wyllie study (13).

#### SOME CURRENT AND PROPOSED RESEARCH ACTIVITIES

It is evident that the US EPA used acute toxicity data to establish a guideline value for copper in water, whereas the WHO relied on information on total copper intake and chronic toxicity. In view of the guideline development problems discussed previously, it seems that more investigation is required to generate a more accurate scientific database. Some recent research activities in this area are outlined here, together with ideas for future study.

#### Epidemiologic approaches

Other articles in this supplement address inborn errors of copper metabolism and the now-outmoded use of non-tin-coated copper or brass vessels for milk preparation. Apart from these circumstances, there are no reports suggesting that copper in foods is associated with toxicity in the general population. Therefore, unless copper absorbed into the body from ingested water induces some systemic effect, it is likely that consideration of the acute gastrointestinal effects of copper in drinking water, ie, nausea, vomiting, diarrhea, and abdominal pains, will be the principal driving force in guideline development. For this reason, studies of the emetic response to copper in humans will be important.

#### Acute gastrointestinal effects from potable water

Buchanan et al (29), in a limited epidemiologic study in Lincoln, NE, ascertained by interview the incidence of gastrointestinal disturbance in 147 households and attempted to correlate this with the copper concentration in the houses' drinking water. Initially, there appeared to be an increased incidence when concentrations exceeded 3 mg/L. However, this relation was not confirmed in a nested case-control study, but incongruence of

copper concentrations measured over different time periods complicated this survey (29). Further work is needed along these lines, and should include copper assays at the time of gastrointestinal upset for more meaningful correlations.

Pettersson and Sandström (30), in a project initiated by the Swedish National Food Administration and the National Environmental Administration, surveyed 1176 households in Uppsala and Malmö, Sweden. In  $\approx 10\%$  of these households, copper in water exceeded 2 mg/L. The study will examine cases of noninfectious diarrhea in children aged 9–21 mo and will eventually determine whether there is any association with copper exposure.


#### Acute gastrointestinal effects in organoleptic tests

In volunteer tasting studies, in which copper concentrations of up to 20 mg/L have been given, there is no record of whether acute effects were manifest (4). It would be informative to repeat such trials with the purpose of recording incidence of gastrointestinal upset. Although perhaps ethically contentious, such an approach could at least be applied where permissible copper concentrations are higher than the standard guidelines of 1.3–2.0 mg/L, eg, in Australia, where up to 5 mg/L is allowed in certain beverages (31).

The thresholds for taste and for induction of acute gastrointestinal effects of copper can be modified by other fluid components, as illustrated by the lack of metallic taste and absence of acute effects during ingestion of milk preparations boiled in brass vessels (copper concentrations  $\leq 60 \text{ mg/L}$ ) (21; T Müller, personal communication, 1996). Thus, consideration of the copper concentration alone may not be sufficient for a complete risk assessment of copper in drinking water. In this regard, it would be interesting to examine in detail the drinking water supplies in some areas of Massachusetts, where acidic water and copper pipe corrosion result in copper concentrations of 4–10 mg/L, with the water reported to have a slight metallic taste but no acute toxicity (32; IH Scheinberg, personal communication, 1994); acclimatization to high copper concentrations may be evident in these circumstances.

#### DISCUSSION

Although guidelines exist for copper in drinking water, there is currently considerable debate over their scientific validity. I have presented the reasons for this and have outlined some research activities that should improve our understanding of copper toxicity. Generally, although copper is an essential element, copper in water is not needed to fulfill dietary copper requirements. Therefore, where practicable, water treatment technologies should be implemented to minimize the leaching of copper from pipes. One field of research in this area involves understanding bacterial colonization and microbe-induced leaching of copper at inner pipe surfaces (33, 34).

Until the acute toxicity of copper ingested from water is better understood, resulting in more accurate guidelines, it is prudent to consider simple public education strategies in areas where copper concentrations are prone to be elevated. For example, discarding the first draft from drinking water taps after overnight or extended stagnation will usually reduce copper concentrations in the water collected thereafter. Such a practice would also reduce exposure to other heavy metals such as lead that can leach from household plumbing (35, 36). 

I gratefully acknowledge Rolf Pettersson for providing information on the Swedish study of copper ingestion in children (30).

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