

**Rolling revision of the WHO Guidelines for
drinking-water quality**

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**Mineral elements related to
cardiovascular health**

By Leslie M. Klevay and Gerald F. Combs, Jr.



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Mineral Elements Related to Cardiovascular Health

Leslie M. Klevay and Gerald F. Combs, Jr.

Consideration of the characteristics of water as determinants of disease risk is not a new idea. Hippocrates is quoted: "We must also consider the qualities of the waters, for as they differ from one to another in taste in weight, so also do they differ much in their qualities" (Adams 1952). Indeed, the science of epidemiology traces its origin to the 19th century work of Snow who mapped the incidence of cholera in London, showing it to be much higher in areas supplied with a particular water source (Frost 1965).

NUTRITIONAL DETERMINANTS OF HEART DISEASE RISK

Keys (1975) was among the first to notice the great variation in heart disease death rates among various nations. The death rate for men in Finland was 16 times that in Taiwan. Times change and methods vary, but differences still are substantial (Anon. 1987b). For example, the male death rate for ischemic heart disease in Scotland is nearly nine times as great as that in Japan which, in turn, is more than five times that in Guatemala.

Ischemic heart disease (IHD) is often thought of as a hereditary illness because some families have several affected members and other families have none. It seems unlikely, however, that most ischemic heart disease is hereditary for two reasons. First, in the wealthier nations, ischemic heart disease is far too common to be explained on the basis of heredity; nearly one-fourth of all deaths in the US are from IHD (Anon. 1987a) (hereditary illnesses typically occur at

prevalences <5 per 1000 live births (Cleave and Campbell 1966). Second, emigrants from low to high IHD risk nations experience an increase IHD risk (Keys *et al.* 1958; Toor *et al.* 1960; Brown *et al.* 1970; Hankin *et al.* 1970; Harding 2003). This phenomenon is best demonstrated by comparing people of Japanese heritage some of whom immigrated to the US: serum cholesterol, one of the better predictors of heart disease risk, was lowest among farmers in Koga, was greater among doctors in Fukouka and men in Hawaii, and greatest among Japanese Americans born in Los Angeles of immigrant parents (Keys *et al.* 1958).

It is now clear that dietary trace elements are associated with heart disease risk. Knox (1973) found a negative correlation between dietary calcium intake and heart disease risk in England and Wales. Varo (1974) found a highly positive correlation between death rates for ischemic heart disease and the dietary ratio of calcium to magnesium in the European Union. In fact, Finnish children with the highest concentrations of cholesterol in serum, and presumably the highest risk of IHD, consumed significantly less calcium than those with the lowest serum concentrations of cholesterol (Räsänen *et al.* 1978). One of us found that the mortality rate for coronary heart disease in the United States was correlated positively with the ratio of zinc to copper in milk consumed in 47 cities (Klevay 1974). Therefore, it is likely that at least part of the geographic difference in risk may be related to the metabolism of these trace elements that are known to be limiting in many diets.

Environmental measurements of trace elements also are associated with risk. Valentine and Chambers (1976) found the risk of death due to arteriosclerotic heart disease was proportional to the concentration of zinc in reservoirs storing water for nine study areas in Houston. Kodavanti *et al.* (2003) have reviewed associations between cardiovascular morbidity and mortality and air pollution indices, and have implicated particulate matter containing highly bioavailable zinc. They also have produced cardiovascular pathology in rats exposed to similar particles by inhalation. People who eat diets low in copper may be particularly susceptible to harm from air pollution high in zinc (Klevay 2003).

WATER AND HEART DISEASE

Kobayashi (1957) made the first observation on the relationship between the chemistry of river water and the risk of vascular disease, a phenomenon that has

come to be called the "water factor." A literature search revealed that the bulk of the data show lower risk with harder water (Sharrett and Feinleib 1975; Klevay 1980a). Crawford (1972) concluded that the correlation may be causal because of findings from English and Welsh towns which experienced increases in heart disease rates after reducing the hardness of the water supplies. Interest in the hard water phenomenon continues (Lacey and Shaper, 1984; Nerbrand *et al.* 1992; MacPherson and Basco 2000; Kousa *et al.* 2004) although mechanisms are ill-defined.

OTHER ILLNESSES RELATED TO WATER MINERAL CONTENT

Sparrow *et al.* (1982) found pulmonary function to be positively correlated with the concentration of copper in the drinking water in homes of nonsmokers. This observation may be clarified by the finding that lungs of rats (O'Dell *et al.* 1978) and pigs (Soskel *et al.* 1982) deficient in copper are anatomically similar to those of emphysema patients. Cadmium, lead and tin have no known nutritional benefits; however, each has been indicated in the etiology of essential hypertension. Chronic exposures to low levels of cadmium increased blood pressure in rats (Schroeder *et al.* 1968; Perry *et al.* 1977); hypertension in people is more likely at environmental than industrial levels of cadmium (Kopp *et al.* 1982). Blood cadmium concentration is directly related to risk of hypertension in humans (Thind and Fischer 1976). The risk of hypertension appears to be more strongly associated with lead exposures at industrial levels (Egeland *et al.* 1992; Maheswaran *et al.* 1993) than environmental ones (Kromhout *et al.* 1985; Kromhout 1998; Staessen *et al.* 1991; Dolenc *et al.* 1993; Klevay 1996).

HARDNESS GOOD OR SOFTNESS BAD?

Several researchers have shown inverse associations between hard water and IHD risk (Water and Heart Disease, above). Such epidemiologic associations, however, cannot distinguish between the prospect of something harmful in soft water or something protective in hard water. Experimental results would support the latter hypothesis, as they have indicated that calcium (and/or magnesium) can be protective against heart disease. To date, six experiments (Yacowitz

1965; Maibach 1967; Maibach 1968; Carlson *et al.* 1971; Bierenbaum *et al.* 1972; Albanese *et al.* 1973) involving a total of 145 subjects have shown decreases in the concentration of cholesterol in serum of men and women ingesting calcium salts (usually carbonate) as supplements to their usual diets. The daily doses of calcium were in the 1-2 g range.

Some 34 elements have been found to show epidemiologic relationships with ischemic heart disease or to the metabolism of cholesterol or other lipids (Klevay 1996; Klevay 1977a) (Figure 1). This chart has been revised several times; earlier (Klevay 1977b; Klevay 1984; Klevay 1995) articles include numerous references to epidemiology and experiment. Shaded elements are those that may act by either enhancing or inhibiting copper, deficiency of which can produce a wide variety of anatomical, chemical and physiological pathology in the cardiovascular system (Klevay 2000).

The mechanisms by which particular elements or their compounds may affect heart disease risk are not clear, but it is likely that they involve effects on enzymes, hormones and messenger molecules. After all, as Mildvan (1970) observed, more than 27% of known enzymes contain mineral elements and/or require minerals for activity. It has been suggested that chromium may produce some of its effects by potentiating insulin (Pi-Sunyer *et al.* 1984); zinc deprivation decreased serum thymulin and interleukin-2 (Prasad *et al.* 1988); and prostaglandin metabolism appears to be modified by dietary copper (Mitchell *et al.* 1988; Allen *et al.* 1991).

Other mechanisms may involve the complexity of interactions among the various mineral elements. For example, zinc is known to inhibit copper utilization (Klevay 1973; Klevay 1975; Underwood 1977; Klevay 1980b) and increase plasma cholesterol (Klevay 1973; Klevay *et al.* 1994), and cadmium can induce hypercholesterolemia that can be relieved by extra copper (Bordas and Gabor 1982). Lead produced increased urinary losses of copper (Victory *et al.* 1986) and can antagonize copper in hematopoiesis (Klauder and Petering 1977). Pekelharing *et al.* (1994) found that amounts of tin similar to those found in human diets can decrease copper status.

Calcium can modify the utilization of other dietary elements. Romasz *et al.* (1977) fed rats a wide range of dietary calcium; as dietary calcium increased, the concentration of cholesterol in serum decreased, and the concentrations of copper and zinc in liver increased and decreased, respectively, although the dietary concentration of the trace elements was constant. Reeves and Chaney

(2001; 2002) found that a low calcium intake of rats caused increased absorption and retention of cadmium, thereby increasing the potential for cadmium intoxication.

TRACE ELEMENTS IN WATER SUPPLIES

Calcium and magnesium are the main elements that give water its hardness. The correlation coefficient between calcium and hardness in water is about 0.96 (Klevay 1975). Calcium in hard water can be an important dietary supplement (Klevay 1975) because hard water can contribute 175-180 mg of calcium daily (Klevay 1975). Calcium and magnesium in water also are correlated (c0.8) as are magnesium and hardness (c0.9) (Klevay 1975). The inverse correlation between coronary heart disease mortality and magnesium in water is similar to that with calcium (Schroeder *et al.* 1968; Schroeder 1960; Schroeder and Kramer 1974).

Lower intakes of dietary magnesium (less than 186 mg daily) are associated with higher risk of coronary heart disease in the Honolulu Heart Program (Abbott *et al.* 2003). Higher magnesium intakes may improve cholesterol metabolism and prevent cardiac arrhythmia. Low dietary magnesium increased the total concentration of cholesterol in the blood of rats and monkeys (Hellerstein *et al.* 1960; Vitale *et al.* 1963). A "placebo" containing magnesium seemed to produce a decline in the concentration of cholesterol in the sera of men and women (Carlson *et al.* 1971). People who live where the water is soft may be in jeopardy for cardiac arrhythmia if they eat diets low in magnesium (Klevay and Milne 2002; Abbott *et al.* 2003).

Most public water supplies do not contain enough copper to be of appreciable nutritional significance. A survey of the water supplies of the 100 largest US cities (Durfor and Becker 1964) found that 94% contained less than 100 µg copper per liter. At typical rates of consumption (a liter per day), this would add less than 0.1 mg copper to daily intakes. However, water chemistry changes between municipal reservoirs and consumers' taps where greater amounts of the element may be available. Angino (1979) found that 16% of 284 US water samples contained enough copper to add at least 0.2 mg of copper to the daily intakes, and 6% would add 0.5 mg of copper to those intakes. Accordingly, drinking water (1 L per day) in Boston, MA, was estimated to provide 0.46 mg copper daily (Sparrow *et al.* 1982). A study of the drinking water available in Seattle, WA (Sharrett *et al.* 1982), showed that source to supply residents with

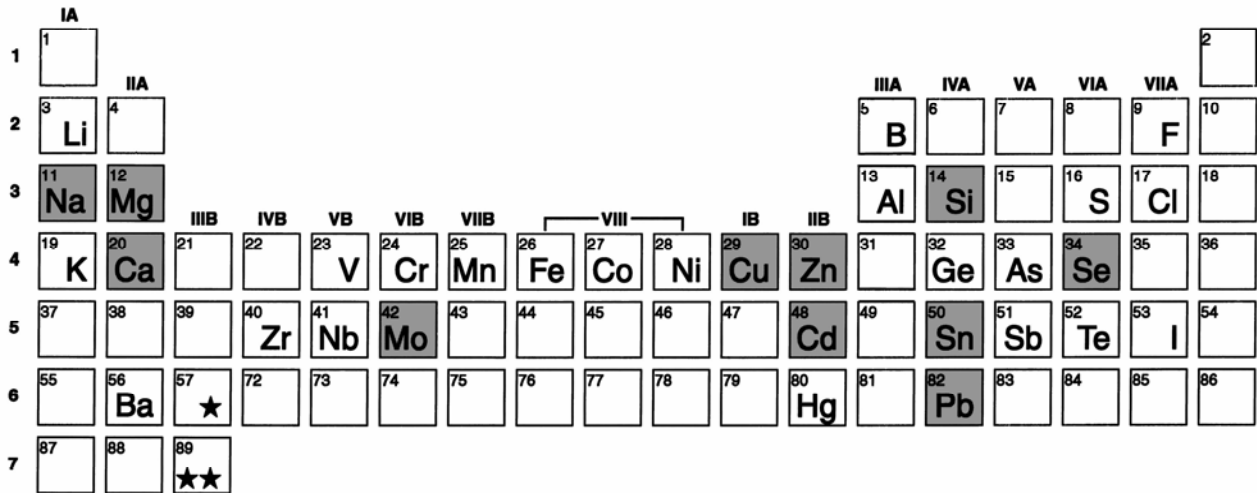
much more copper: 1.3-2.2 mg per day. Copper supplements this large are easily tolerable (Klevay 1984; Araya *et al.* 2001, 2003) and may be beneficial considering that the Western diet often is low in copper (Klevay 1998) and that people with cardiovascular disease have been found to have decreased copper in hearts and arteries (Klevay 2000; Klevay 2002) and decreased activities of enzymes dependent on copper (Klevay 2002). A diet low in copper can increase cholesterol in plasma (Klevay *et al.* 1984).

CONCLUSION

In most cases, drinking and cooking water may be of only minor importance to the trace element nutrition of individuals. In some cases, and particularly for individuals dependent on foods and food systems that do not provide adequate amounts of calcium and copper, some water sources by virtue of their hardness and/or contributions of copper piping, can provide significant amounts of those elements. Available information indicates that such sources can be beneficial. We conclude that hard water is good because it contains nutrients valuable in themselves and because these nutrients can decrease impact of toxic elements in the environment.

To minimize heart disease risk, the ideal water should contain sufficient calcium and magnesium to be moderately hard. No effort should be made to eliminate trace elements such as copper and iron where these elements are in short, dietary supply. Elements such as cadmium and lead, which can accumulate in the body, should be minimized.

Elements of Atherosclerosis



Klevay, *Perspect. Biol. Med.* 20:186, 1977; *Adv. Nutr. Res.* 1:227, 1977; CRC Press, 1984; Smith-Gordon, 1995; CRC Press, 1996.

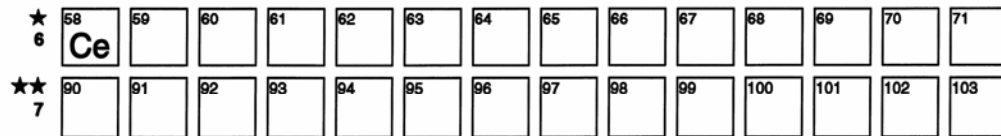


Figure 1. Elements implicated in atherosclerosis or ischemic heart disease by epidemiology or experiment.

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