APPENDIX No. 11 (Expert Reasons REF 6)

REF 6 of the „EXPERT REASONS for existence of bottled infant water as an independent category" document

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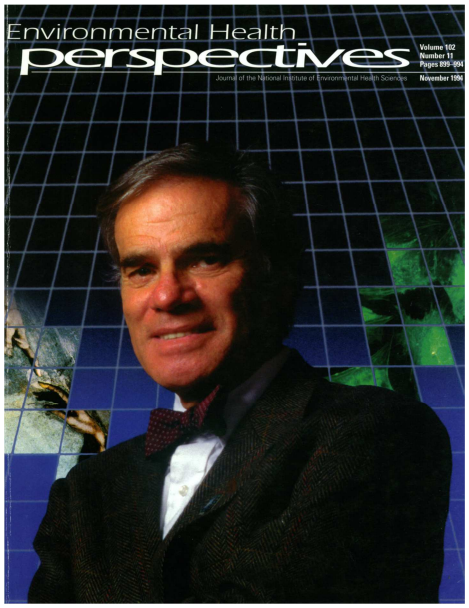

Gastrointestinal Upsets Associated with Ingestion of Copper-contaminated Water

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During 1992 and 1993 the Wisconsin Division of Health investigated five cases in which copper-contaminated drinking water was suspected of causing gastrointestinal upsets. Each of these case studies was conducted after our office was notified of high copper levels in drinking water or notified of unexplained illnesses. Our findings suggest that drinking water that contains copper at levels above the federal action limit of 1.3 mg/l may be a relatively common cause of diarrhea, abdominal cramps, and nausea. These symptoms occurred most frequently in infants and young children and among residents of newly constructed or renovated homes. *Key words*: copper, cramps, diarrhea, drinking water, nausea. *Environ Health Perspect* 102:958–961 (1994)

Copper is an essential element in the human diet. According to the Total Diet Study (*1*), which was completed by the U.S. Food and Drug Administration in 1986, daily intakes for infants 6–11 months old, 2-year-old children, and adults average 0.45, 0.57, and 1.2 mg, respectively. Dietary copper comes from red meats, green leafy vegetables, and seeds and grains. Since most natural water sources contain less than 10 µg of copper/liter (*2*), drinking water does not normally contribute significant amounts of dietary copper. However, corrosion of copper plumbing materials can significantly increase copper levels in household water supplies.

In November 1985, the U.S. Environmental Protection Agency proposed a maximum contaminant level goal (MCLG) of 1.3 mg/l for copper in public drinking water (*3*). This standard, which was adopted in 1991 (*4*), is based on a 1957 report written by Canadian physician John Wyllie (*5*). Wyllie's report described symptoms of nausea, vomiting, abdominal cramps, headaches, dizziness, and diarrhea that afflicted 15 nurses who became ill less than an hour after they consumed 0.75–4.5 ounces of an alcoholic beverage that had been refrigerated in a copper-lined flask. Based on a re-creation of this event, these women had copper intakes of 5.3–32 mg. To develop the MCLG of 1.3 mg/l, the lowest effective dose of 5.3 mg was divided by an uncertainty factor of 2 to derive an adjusted acceptable daily intake (AADI) of 2.65 mg copper, and daily ingestion of 2 l of water was assumed.

Only a few cases of drinking-water-induced copper intoxication appear in the literature. In 1979, Stenhammer (*6*) described prolonged diarrhea, slow weight gain, and elevated serum and urinary copper levels in three Swedish children (ages 1–2.5 years) whose household water supplies contained copper levels ranging from 0.22 to 1.1 mg/l. Two of these cases involved newly constructed homes. The third case involved an older home in which new copper plumbing was installed during renovation. In 1984 Spitalny et al. (7) reported that a 32-year old Vermont man and his daughters experienced recurrent episodes of vomiting and abdominal pain after moving into a new home. These symptoms stopped after laboratory tests revealed copper levels of 2.8–7.8 mg/l in water samples from the home and the family was advised not to drink their water. In a 1989 report, Pettersson and Kjellman (*8*) reported higher rates of vomiting, diarrhea, colic, and constipation in 19 children who drank water that contained more than 1.0 mg/l copper.

During 1992 and 1993 the Wisconsin Division of Health investigated five incidents in which copper-contaminated drinking water was suspected of causing illness. These investigations involved people of varying ages with various lengths and levels of exposure. Our study methods were designed to determine whether the reported illnesses could be associated with daily copper intake estimates and whether infants and children were more sensitive to the acute effects of ingested copper than adults.

Methods

Five independent case studies were conducted by the Wisconsin Division of Health in cooperation with local public health departments. Two of these were initiated after unexplained gastrointestinal upsets were reported. The remaining investigations were done after elevated copper levels were detected in public drinking water supplies.

We collected water samples in accordance with procedures described in the National Primary Drinking Water Regulations for Lead and Copper (*4*). These regulations require that copper analyses be done on water samples collected after the water has been allowed to stand in the pipes for at least 6 hr. Except as noted, all copper analyses were conducted by certified laboratories according to EPA method 200.7 (*9*).

Health data for case study I was obtained by interviewing the infant's mother and from hospital records. All other data were collected using self-administered questionnaires. Information about age, weight, general health status, frequency of gastrointestinal symptoms, water use habits, and exposure duration were requested.

We used completed questionnaires and water quality data to assess the association between copper exposure and illness rates. For statistical comparison, respondents were classified as "ill" if they had experienced intermittent or constant symptoms of diarrhea, abdominal cramps, or nausea. Individuals who did not report these symptoms or who experienced them only once were classified as "not ill." Relative risk ratios (RRs), confidence limits, and *p*-values were calculated using Epi-Info software provided by the U.S. Centers for Disease Control, Atlanta, Georgia.

Case Summaries

Case Study I. Failure to Thrive, Dehydration, and Methemoglobinemia in an Infant

A female infant born weighing 7 lb, 9 oz (3.4 kg) appeared well during her first month at home (*10*). During her third week of life she developed diarrhea and began to vomit after feedings. At 6 weeks of age she was hospitalized for treatment of vomiting, failure to thrive, and dehydration secondary to vomiting. On admission she weighed 6 lb, 10 oz. (3.0 kg) and was afebrile with no other signs of infection. The infant was rehydrated with oral fluids, returned to her soy-based formula which she tolerated well, and released the following day. After returning home, her symptoms recurred and she was readmitted to the hospital 6 days after her initial release with a principal diagnosis of failure to thrive. Secondary diagnoses were vomiting, poor weight gain, and methemoglobinemia. Blood tests revealed a hemoglobin level of 13.0 g/dl (normal, 9–14 g/dl), with 21.4% methemoglobin (normal, 0–3%). After 24-hr treatment with

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oral fluids and oxygen, her methemoglobin level dropped to 11.1%. After being stabilized, the infant was transferred to a referral center for a complete medical evaluation. No underlying medical problems were identified, and she was released 10 days after her second admission. At that time the family began using bottled water to dilute her liquid-concentrate formula. The child's symptoms did not recur, and she appeared healthy at her 9-month checkup.

Inspection of this family's rural home found that the water was supplied by a shallow sandpoint well. A reverse-osmosis (R/O) unit installed in the basement served a separate faucet in the kitchen sink. At the time of the infant's first hospitalization, the nitrate-N levels in the R/O-treated and untreated water were 9.9 and 58.0 mg/l, respectively (EPA MCLG, 10.0 mg/l). Additional water quality tests conducted approximately 6–8 weeks after the infant's second recovery revealed a nitrate-N level of 38.8 mg/l, a pH of 6.19, and an alkalinity of 16 mg/l. A sample from the reverse-osmosis unit contained an nitrate-N concentration of 23.5 mg/l. Early morning and midday water samples from the kitchen sink contained 7.8 and 0.16 mg/l copper, respectively. Analysis for other metals and agricultural pesticides failed to detect any other violations of federal or state drinking water standards, and the water was free of coliform bacteria. Based on our review of the medical history and the water quality information, it was considered likely that this infant's persistent vomiting and diarrhea, which led to weight loss and dehydration, were caused by prolonged exposure to copper-contaminated drinking water that was used to dilute her formula. In addition, her elevated methemoglobin level was consistent with exposure to nitrate-contaminated water.

Case Study II. Gastrointestinal Upsets Suffered by Residents of New Homes

Between January and June of 1992, several residents of a new subdivision developed flu-like symptoms shortly after moving into their homes. Their illnesses were characterized by nausea, diarrhea, vomiting, and abdominal cramps. Many residents attributed their illnesses to their household water that was supplied by a community well. Some said that their water appeared blue and left blue stains on bathroom fixtures and laundry items. Because of these concerns, the municipal water supplier analyzed copper levels in several water samples from these homes and from other points in the distribution system. These tests revealed copper levels of 0.09 and 0.16 mg/l in samples from two homes located in other neighborhoods, 0.31 to 0.44 mg/l in samples from homes where illnesses had been reported, and 12.0 mg/l in a sample from an underground water pipe serving a home in the subdivision. To further evaluate exposure to water-borne copper, the families in this subdivision submitted water samples to a private laboratory for analysis during July. Copper levels in these samples ranged from 0.29 to 1.2 mg/l (mean 0.54).

In response to continued water-quality complaints, the local health department distributed questionnaires and water testing kits to each home in this subdivision during August. The questionnaires sought information about age, general health status, residence history, daily water consumption, water collection practices, and the frequency of several symptoms including diarrhea, vomiting, nausea, abdominal cramps, headaches, and irritability.

Early morning first-draw water samples collected from the cold water tap of each household were free of fecal coliform bacteria and had copper concentrations that ranged from 0.16 to 0.65 mg/l. Surveys completed for 27 adults and 15 children indicated that 24 of the 42 residents (57%) in 9 of the 14 households had experienced episodes of diarrhea, abdominal cramps, or nausea since moving into their home. Among those reporting symptoms, four children and two adults also reported episodes of vomiting, six preschool-aged children were described as unusually irritable, and five adults and four children had recurrent headaches.

The most important predictors of illness were the ingestion of first-draw water, the date the home was occupied, and the age of the respondent (Table 1). Residents who consumed first-draw water were five times more likely to report previous gastrointestinal upsets than residents who drank bottled water, water from flushed faucets, or prepared beverages. Residents who moved into their homes before May 1 were twice as likely to report symptoms as residents who moved in after that date (86% versus 43%), and the prevalence of symptoms was higher among residents under the age of 18 with episodes of diarrhea or abdominal pain reported by 80% of the children and 44% of the adults.

At the time of the survey, only six residents were consuming first-draw water, and none of the residents were ill. No association was found between the historical prevalence of gastrointestinal disturbances and copper levels that were measured at the time of the investigation. However, since several residents indicated that water quality had improved before our investigation and the illnesses were no longer occurring, the lack of correlation could not exclude the possibility that these illnesses may have been caused by ingestion of copper-contaminated water.

Case Study III. Health Survey in a Community with Corrosive Water

Water supply testing required under the Safe Drinking Water Act found that copper levels in one community (population 3300) ranged from 0.09 to 5.32 mg/l and that 27 of the 40 homes included in the testing had copper levels above the federal MCLG of 1.3 mg/l. Because of this finding, health questionnaires were distributed to the residents of these homes. Sixty residents from 37 homes completed the questionnaires, providing information about residence history, age, general health status, daily water consumption, water collection practices, and the frequency of several symptoms including diarrhea, vomiting, nausea, abdominal cramps, and headaches. In addition, a family of five whose water was tested by the county health department also completed questionnaires.

Survey respondents ranged in age from 15 months to 91 years (mean 52 years). More than 80% of the respondents had lived in their homes for more than 5 years, and 94% of those who provided information about water collection methods reported routinely flushing their pipes before collecting water for drinking or food preparation. Only seven residents reported episodes of nausea, abdominal pain, or diarrhea (Table 2). Among these were a 37-year-old woman and her teenaged son who attributed their symptoms to the flu, and a 64-year-old woman whose symptoms were apparently caused by a milk allergy. Early morning water samples from the homes of these residents contained 3.8 and 3.3 mg copper/l,

Table 1. Case study II: gastrointestinal upsets in residents of new homes

	No. of respondents			
	Total	ILL	RR (95% CI)	*p*-value[a]
Age of respondent				
<18 years	15	12	1.80 (1.10–2.94)	0.027
>18 years	27	12		
Date of occupancy				
Before May 1	14	12	2.00 (1.24–3.23)	0.009
After May 1	28	12		
Drinking water				
First draw	24	21	5.25 (1.85–14.91)	0.000
Flushed	18	3		

RR, relative risk.
[a]Mantel-Haenszel *p*-value.

Table 2. Case study III: community with corrosive water

	No. of respondents			
	Total	ILL	RR (95% CI)	*p*-value[a]
Age of respondent				
<18 years	14	4	4.86 (1.23–19.21)	0.015
>18 years	51	3		
Residency time				
<1 year	9	4	8.30 (2.21–31.09)	0.000
>1 year	56	3		
Drinking water				
Flushed	32	7		
First draw	2	0	—	—
Not known	31	0		

RR, relative risk.
[a]Mantel-Haenszel *p*-value.

respectively. The only other residents who reported symptoms were a 22-year-old woman and her children, aged 15 months, 3 years, and 4 years. This family became ill shortly after moving into a renovated apartment with new copper plumbing and recovered after being advised to drink bottled water. A first-draw water sample collected at the time of their illnesses had a copper concentration of 5.3 mg/l.

Case Study IV. Blue Water in a University Science Building

During the fall semester of 1992, a university employee noticed that water from a drinking fountain in a new wing of the science building had a faint blue color. As a result, water samples from several fountains and sinks in the building were tested for copper levels by the chemistry department and verified by a certified laboratory. Samples from nine fountains located in the new wing ranged from 1.6 to 7.7 mg/l (mean 4.4 mg/l). Five fountains located at the west end of the new wing had the highest copper levels. Water from those fountains had copper concentrations of 5.0, 5.2, 6.2, 7.5, and 7.7 mg/l. Copper levels in water from four fountains in the old wing were below the federal MCLG of 1.3 mg/l and ranged from 0.4 to 1.1 mg/l. Water samples from five bathroom sinks contained acceptable copper levels of 0.01 to 0.62 mg/l. Based on these results, five fountains at the west end of the new wing were removed. This action caused concern among some workers in the building about the health effects of copper.

To determine whether any illnesses had resulted from ingestion of the copper-contaminated water, health questionnaires were distributed to the employees. Information regarding age, general health status, the number of years and hours/week spent in the building, the frequency of gastrointestinal upsets, and water consumption was collected. Water consumption questions were intended to determine the average number of cups of water consumed during each workday, the source (sink versus fountain, floor, and wing), and the form in which it was consumed; e.g., as water, coffee, tea, or prepared foods.

Forty-one questionnaires were returned from an estimated 75 building occupants. Respondents included 17 women and 24 men who ranged in age from 27 to 67 years (mean 47.5). Water consumption information provided by the survey and measured copper levels were used to estimate a daily copper intake from water for each respondent. These estimates ranged from 0 to 3.8 mg/day and were significantly correlated with the prevalence of gastrointestinal symptoms (Table 3). Of 26 employees who had estimated daily intakes ≤0.55 mg (mean 0.15 mg), only three reported gastrointestinal symptoms. In comparison, 8 of 14 individuals whose estimated daily intakes were greater than 0.55 mg reported episodes of nausea, diarrhea, or abdominal cramps.

Symptom prevalence was also correlated with the drinking water source and patterns of water consumption (Table 3). Just 1 of 11 workers who drank only coffee or tea that was prepared using water from a sink reported gastrointestinal upsets. Conversely, 10 of 28 employees (36%) who drank water obtained from the drinking fountains reported episodes of diarrhea and abdominal cramps. Similarly, workers whose primary water source was located in the new wing reported symptoms more frequently than those who consumed water from the old wing of the building.

Case Study V. Bitter-tasting Water in an Apartment Building

In response to a drinking water taste complaint, the local health department inspected an eight-unit apartment building and collected several water samples for analysis. The building was constructed in 1970 and was served by a private well. Water-quality analyses revealed very low alkalinity (5.5–9.9 mg/l as $CaCO_3$), hardness (17.1 mg/l) and pH (5.2) readings. Early morning first-draw water samples from six apartments had copper levels that exceeded the federal MCLG of 1.3 mg/l.

Questionnaires asking for information about residential history, water use practices, and health status were completed for 13 adults and 6 children. Several individuals stated that their water tasted and smelled "bad," had a "bitter taste," and left "green stains in the sink and tub." Daily water consumption ranged from 2 to 6 cups for children, and from 1 to 10 cups for adults. Daily copper intake estimates from water ranged from 0.5 to 8.1 mg (mean 3.4 mg).

Eighty percent of the residents (15/19) experienced intermittent bouts of abdominal cramps, diarrhea, nausea, or vomiting since moving into the building. Ten residents recalled feeling better when they were away from home or when they drank bottled water. Gastrointestinal upsets were more prevalent in children and in those who drank first-draw water (Table 4). Two mothers listed "tummy cramps" and diarrhea as chronic illnesses suffered by their children. One wrote the following comment: "[My son] was born right after we moved . . . here. He always threw up his formula in large quantities. He was tested for a [bowel] obstruction . . . but the tests came back negative. Since having found out about the water, [he] only drinks bottled water and his stomach aches have stopped. If . . . we had known this five

Table 3. Case study no. IV: blue water in a university science building

	No. of respondents			
	Total	ILL	RR (95% CI)	*p*-value[a]
Age of respondent				
<18 years	0	0	—	—
>18 years	40	11		
Daily copper intake				
0.00–0.55 mg	26	3		
0.60–3.80 mg	14	8	4.95 (1.56–15.75)	0.002
Drinking water				
None	2	0		
Sink	11	1		
Fountain	28	10	4.64 (0.66–32.55)	0.063
Source location				
Old wing	16	3		
New wing	25	8	1.71 (0.53–5.49)	0.356

RR, relative risk.
[a]Mantel-Haenszel *p*-value.

Table 4. Case study no. V: bitter-tasting water in an apartment building

	No. of respondents			
	Total	ILL	RR (95% CI)	*p*-value[a]
Age of respondent				
<18 years	7	6	1.14 (0.73–1.78)	0.591
>18 years	12	9		
Daily copper intake (adults only)				
0.9–3.0 mg	5	4		
3.1–8.1 mg	7	5	0.89 (0.47–1.70)	0.746
Drinking water				
First draw	4	4	1.36 (1.00–1.85)	0.258
Flushed	15	11		
Copper level				
<3.0 mg/l	10	9		
>3.0 mg/l	9	6	0.74 (0.45–1.23)	0.225

RR, relative risk.
[a]Mantel-Haenszel *p*-value.

years ago it would have saved a lot of trips to the doctor . . ." Based on the water test results, the local health department recommended that the building owner take action to reduce the corrosiveness of the water supply and that tenants consume bottled water until the problem was corrected.

Discussion

Our findings from five independent case studies suggest that prolonged ingestion of copper-contaminated drinking water may be a relatively common cause of stomach upsets, abdominal cramps, and diarrhea. This information is consistent with previously published reports. The youngest participant in these case studies was a 6-week-old female who was hospitalized after experiencing prolonged diarrhea and vomiting. These symptoms resolved during her first hospitalization and recurred when she returned home. Water samples collected from her home contained copper levels of 0.16–7.8 mg/l. Her illness ended after her parents were advised to use bottled water to prepare her formula. This case is similar to those Stenhammar (*6*) described in which three Swedish children became ill after consuming water that contained copper levels of 0.22–1.1 mg/l.

In case studies II and III, children appeared to be more sensitive to the acute effects of copper ingestion than adults. The higher prevalence of symptoms in children may have resulted from higher copper exposures per unit body weight or from a greater sensitivity of children to the irritant effects of ingested copper. Recall bias should also be considered in interpreting these results, however, as parents who were concerned about the illness of an infant or child may have been more likely to report that event than others.

Most of these cases involved drinking water supplies that contained copper levels above the federal standard of 1.3 mg/l. First-draw water samples in most of the homes or offices where illnesses occurred exceeded 3 mg/l. Case study II involved lower copper levels; however, the illnesses described in that case occurred up to 8 months before our investigation, and water quality analyses conducted by the water supplier soon after the first illnesses were reported revealed copper levels ranging from 0.09 to 12.0 mg/l. Therefore, the illnesses may have been caused by intermittent high copper levels that were present for a brief period while the water distribution system and household plumbing were new. Support for an association between exposure to waterborne copper and gastrointestinal illness was provided by the observation that symptoms were reported more frequently by residents who drank first-draw water.

The effectiveness of flushing faucets to reduce copper exposure was also demonstrated in case studies III and IV. In case study III, most of the community residents routinely flushed their faucets before collecting drinking water, and very few individuals reported gastrointestinal symptoms even though first-draw copper levels exceeded the federal action level in 67% of the homes surveyed. Likewise, in case study IV, university workers who drank water from bathroom sinks reported fewer symptoms than co-workers who drank water provided by seldomly used fountains. Copper levels were lower in water collected from the sinks, presumably because of frequent use. In contrast to these findings, most of the apartment residents in case study V suffered gastrointestinal upsets regardless of their water collection habits. The failure of flushing faucets for a minute or two to protect these individuals may have been due to the apartment building's size or to other water supply characteristics, as the effectiveness of this procedure depends on the length and diameter of the pipes being flushed, the water flow rate, and the flushing time.

Four of our investigations were based on data from self-administered questionnaires that could not be verified by medical records. Findings from these cases may have been affected by over- or underreporting of symptom rates by the survey respondents and by higher response rates among residents who were concerned about a previous illness or about their water supply. This inherent weakness is unavoidable in environmental health investigations that assess the incidence of self-reported symptoms and may preclude the use of such studies for some purposes. Even so, these case studies provide additional evidence that ingestion of copper-contaminated drinking water may pose a significant threat to the well-being of infants and young children and may also cause transient discomfort in adults. These findings are consistent with previous reports and underscore the importance of community awareness and water quality assurance. In addition, they should encourage health care providers to consider copper intoxication in the differential diagnosis of unexplained gastrointestinal illnesses, particularly when these occur in conjunction with a change in the drinking water supply.

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