ACUTE FLUORIDE POISONING FROM A PUBLIC WATER SYSTEM

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Abstract *Background.* Acute fluoride poisoning produces a clinical syndrome characterized by nausea, vomiting, diarrhea, abdominal pain, and paresthesias. In May 1992, excess fluoride in one of two public water systems serving a village in Alaska caused an outbreak of acute fluoride poisoning.

Methods. We surveyed residents, measured their urinary fluoride concentrations, and analyzed their serum-chemistry profiles. A case of fluoride poisoning was defined as an illness consisting of nausea, vomiting, diarrhea, abdominal pain, or numbness or tingling of the face or extremities that began between May 21 and 23.

Results. Among 47 residents studied who drank water obtained on May 21, 22, or 23 from the implicated well, 43 (91 percent) had an illness that met the case definition, as compared with only 6 of 21 residents (29 percent) who drank water obtained from the implicated well at other times and 2 of 94 residents (2 percent) served by the other water system. We estimated that 296 people were poisoned; 1 person died. Four to five days after the outbreak, 10 of the 25 case patients who were tested, but none of the 15 control subjects, had elevated urinary fluoride concentrations. The case patients had elevated serum fluoride concentrations and other abnormalities consistent with fluoride poisoning, such as elevated serum lactate dehydrogenase and aspartate aminotransferase concentrations. The fluoride concentration of a water sample from the implicated well was 150 mg per liter, and that of a sample from the other system was 1.1 mg per liter. Failure to monitor and respond appropriately to elevated fluoride concentrations, an unreliable control system, and a mechanism that allowed fluoride concentrate to enter the well led to this outbreak.

Conclusions. Inspection of public water systems and monitoring of fluoride concentrations are needed to prevent outbreaks of fluoride poisoning. (N Engl J Med 1994;330:95-9.)

SINCE the late 1940s, many communities in the United States have adjusted the fluoride concentration in their water systems to prevent dental caries.[1] Numerous studies attest to the effectiveness and safety of maintaining fluoride concentrations in the range recommended by the Public Health Service — 0.7 to 1.2 mg per liter.[2,3] As of 1989, a total of 9411 public water systems in the United States provided fluoridated drinking water to 135 million people,[4] yet only six outbreaks of acute fluoride poisoning related to overfluoridation have been reported.[5-10] Acute fluoride poisoning caused the death of one patient in Maryland[8] and, recently, of three patients in Illinois (Flanders R, Illinois Department of Public Health: personal communication), all of whom were undergoing dialysis therapy. In this paper we describe an outbreak of acute fluoride poisoning resulting from overfluoridation of a public water system.

METHODS

Background

Hooper Bay, Alaska, is a small village on the Bering Sea populated predominantly by Alaska Natives. The village has two geographically distinct sections with separate wells and water systems: sections 1 (population, 470) and 2 (population, 375). Neither water system provided running water to individual homes; residents carried water from holding tanks to their homes, where it was stored for domestic use. On May 26, 1992, the Alaska Division of Public Health was notified of an outbreak of acute gastrointestinal illness in the village. The water system in section 1 had been turned off on May 23 after staff members at the Hooper Bay health clinic noted that many residents had become ill shortly after drinking water from that system. Since acute fluoride poisoning produces a clinical syndrome characterized by nausea, vomiting, diarrhea, abdominal pain, and paresthesias and because tests conducted during the six weeks before the outbreak had shown fluoride concentrations in water system 1 of 6.5 and 20.0 mg per liter, acute fluoride poisoning was suspected.

The outbreak resulted in one serious illness and one death. On May 23, a 37-year-old woman with a two-day history of vomiting and diarrhea was evacuated by air to a regional hospital. Her serum calcium concentration was 5.2 mg per deciliter (1.3 mmol per liter), and her serum fluoride concentration was 9.1 mg per liter (480 μmol per liter) (the normal fasting serum fluoride concentration in persons using drinking water containing 1 mg of fluoride per liter is 0.01 to 0.03 mg per liter [0.5 to 1.6 μmol per liter]). She recovered without apparent sequelae. On May 23, after 24 hours of intractable vomiting, a 41-year-old man was found dead at home. He had attempted to remain hydrated by drinking an estimated 10 liters of water from water system 1 on May 21 and 22. His only known medical problem was peptic ulcer disease, for which he took cimetidine. The postmortem serum calcium concentration was 4.9 mg per deciliter (1.22 mmol per liter), and the urinary fluoride concentration (not corrected for creatinine content) was 55 mg per liter (2900 μmol per liter).

Epidemiologic Study

To determine the duration of the outbreak, we reviewed the health clinic records of all patients seen from May 1 to May 25 with nausea, vomiting, diarrhea, or abdominal pain. Of 31 patients with these symptoms, 22 were seen on May 21, 22, or 23. We therefore defined a case patient with fluoride poisoning as a resident who had at least one of the following symptoms on May 21, 22, or 23: nausea, vomiting, diarrhea, abdominal pain, or numbness or tingling of the face or extremities.

On May 27 we went to the clinic and asked patients who were seen there on May 21, 22, or 23 to come to the clinic with any available family members. These persons, as well as patients being seen at the clinic for any reason on May 27, were interviewed as described below. On May 28 we identified case patients (and control subjects) through a household survey conducted by starting at one randomly selected household in each section of the village and walking door to door until residents of 15 households in section 1

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Supported in part by grants (DE-06113 and DE-06429) from the National Institute of Dental Research, National Institutes of Health.

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and 17 households in section 2 had been interviewed. We collected information on all residents of each household, and adult residents were asked to provide information about anyone not at home. Since case patients identified at the clinic and through the household survey were similar with respect to age and onset, duration, and type of symptoms, we considered all case patients together.

All residents interviewed on May 27 or 28 responded to a questionnaire that included questions about symptoms and water consumption. Information about persons under 18 years of age was obtained from a parent or guardian. Some residents had difficulty recalling the details of their illness or their water consumption; results are given only for those able to recall the details.

To evaluate risk factors and calculate attack rates, we conducted a case–control study and a retrospective cohort study. The case–control study analyzed the case patients and control subjects who were interviewed at the clinic on May 27; it compared the characteristics of persons meeting the definition of a case patient with those of persons who did not. All persons interviewed on May 27 who did not meet the case-patient definition were considered controls for this analysis. The retrospective cohort study analyzed the case patients and control subjects identified during the household survey. Since almost all the acutely ill persons lived in section 1, we used the cohort study to estimate the total number with fluoride poisoning.

Biochemical Measurements

On May 27 and 28, we collected blood and spot urine specimens from 20 case patients and blood or urine alone from 7 case patients. Urine specimens were also collected from 15 control subjects, 3 of whom also provided a blood sample. Urine was analyzed for fluoride and creatinine. Serum was analyzed for fluoride and, in most cases, aspartate aminotransferase, calcium, creatine kinase, lactate dehydrogenase, magnesium, and phosphorus.

Follow-up urine specimens were collected from case patients with the highest initial urinary fluoride concentrations. Six case patients provided a specimen on June 5 or June 9, and three provided specimens on both dates. On June 9 follow-up blood specimens were collected from 11 case patients who had an abnormal result on serum-chemistry testing or an elevated serum fluoride concentration.

Urinary fluoride was measured by direct ion-specific electrode potentiometry and corrected for the creatinine content by dividing the measured fluoride concentration (in milligrams per liter) by the urinary creatinine concentration (in milligrams per deciliter) and then multiplying the value by 100 mg per deciliter. Serum fluoride was measured in the same manner after overnight diffusion by the hexamethyldisiloxane-facilitated technique.[11]

Environmental Investigation

We reviewed the records of routine fluoride determinations for the Hooper Bay water systems and collected water samples from the two systems and from residents who still had water from system 1 in their homes. The Alaska Department of Environmental Conservation inspected both water systems and had water samples analyzed for fluoride using protocols approved by the Environmental Protection Agency.

Dose Estimates

To estimate the dose of fluoride ingested, we asked each case patient to recall how much water he or she had consumed that had been obtained from system 1 from May 21 to 23. Beverages made with water were included in the calculation, but water consumed in food was not. The estimated dose was calculated as the volume of water consumed (in liters) multiplied by the presumed fluoride concentration of the water (in milligrams per liter) divided by body weight (in kilograms). The presumed fluoride concentration was based on the results of the environmental investigation.

Statistical Analysis

Odds ratios, relative risks, and 95 percent confidence intervals were calculated with the Epi Info program.[12] Pearson's correlation coefficients were determined by the least-squares method[13]; we report corresponding two-tailed P values. The confidence interval for the estimated number of section 1 residents with fluoride poisoning was calculated according to the method of Levy and Lemeshow.[14]

Results

Epidemiologic Study

Overall we identified 91 case patients; all were Alaska Natives, ranging in age from 6 months to 73 years (median, 21 years), and 51 percent were female. The most common symptoms were nausea, vomiting, and abdominal pain (Table 1). All case patients had stopped drinking water from system 1 by May 23. Most case patients began to have symptoms on May 22 (Fig. 1). The median interval between the consumption of water and the onset of symptoms was 7 minutes (range, <1 to 150), and the median duration of symptoms was 24 hours (range, 1 to 132).

There were 42 case patients and 54 control subjects in the case–control study. As compared with the controls, the case patients were 7 times more likely to live in section 1, 18.5 times more likely to consume water from water system 1, and 76 times more likely to have consumed water obtained from water system 1 on May 21, 22, or 23 (Table 2).

There were 175 persons in the retrospective cohort study. The attack rates among residents of sections 1 and 2 were 63 percent and 2 percent, respectively (Table 3). Among residents of section 1, the attack rate among those who usually drank water from system 1 was 71 percent, whereas among those who drank water obtained from system 1 from May 21 to 23, the attack rate was 91 percent (Table 3). Six residents of section 1 who were sick but who had not drunk water collected from system 1 on May 21, 22, or 23 recalled drinking water obtained on May 20. The attack rate among the residents of section 1 implies that 296 of the 470 residents (63 percent) had acute fluoride poisoning (95 percent confidence interval, 249 to 343).

Biochemical Measurements

For specimens collected on May 27 or 28, the median urinary fluoride concentrations in case patients and control subjects were 3.4 mg per liter (180 μmol per liter) and 1.7 mg per liter (89 μmol per liter), respectively. Ten case patients and no control subjects had elevated urinary fluoride concentrations (>5.0 mg per liter [>260 μmol per liter]). The median serum fluoride concentrations were 0.067 mg per liter (3.5 μmol per liter) in the case patients and 0.029 mg per liter (1.5 μmol per liter) in the control subjects. The serum fluoride concentrations in the case patients correlated strongly with the duration of illness ($r = 0.84$, $P<0.001$).

The median urinary fluoride concentrations in case patients retested on June 5 and 9 were 6.4 mg per liter (340 μmol per liter) and 4.4 mg per liter (230 μmol per liter), respectively. The urinary fluoride concentra-

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Table 1. Symptoms of 91 Case Patients with Acute Fluoride Poisoning in Hooper Bay, Alaska, in May 1992.

SYMPTOM	PERCENT AFFECTED
Nausea	90
Vomiting	80
Abdominal pain	52
Diarrhea	23
Loss of appetite	13
Headache	11
Weakness	10
Itching	9
Numbness or tingling of an extremity	4
Shortness of breath	4
Fatigue	4

tions decreased consistently from May 27 or 28 to June 9; for the persons retested on both June 5 and 9, the decrease was nonlinear.

All 14 case patients tested on May 27 or 28 had an elevated serum lactate dehydrogenase concentration (median, 152 U per liter). Eleven case patients had elevated serum aspartate aminotransferase concentrations, eight had hypomagnesemia, three had hyperphosphatemia, and one had an elevated creatine kinase concentration. All serum calcium values were normal. Serum lactate dehydrogenase concentrations correlated with the urinary ($r = 0.74$, $P = 0.002$) and serum ($r = 0.57$, $P = 0.004$) fluoride concentrations obtained on May 27 or 28. Among 11 case patients retested on June 9, 6 had hypomagnesemia, 3 had hyperphosphatemia, and 1 had an elevated serum lactate dehydrogenase concentration; the median serum fluoride concentration was 0.086 mg per liter (4.5 μmol per liter).

Environmental Investigation

Water system 1 included a 6340-liter (1675 gal) holding tank, two 95-liter (25 gal) chemical vats (for chlorine and fluoride concentrates), a water pump and two chemical feed pumps, high and low floats connected to an electrical control system to regulate the volume of water in the holding tank, and a public watering point outside the well house (Fig. 2). Regulations requiring that results of monthly fluoride measurements be submitted to the state had been unmet for almost two years. The operator lacked formal training and could not correctly perform fluoride tests. High fluoride concentrations were documented in January 1991 (7.3 mg per liter) and again six and three weeks before the outbreak (6.5 and 20 mg per liter, respectively). After the third report of an elevated fluoride concentration, local health officials asked the water-system operator to drain the holding tank and unplug the fluoride pump. On May 26, 1992, however, the fluoride pump was still operating. Water obtained from water system 1 by residents on May 20 and 21 had fluoride concentrations of 2 and 150 mg per liter, respectively; water obtained on May 27 had a fluoride concentration of 58 mg per liter. Water obtained from system 2 on May 27 had a fluoride concentration of 1.1 mg per liter.

Major electrical and mechanical defects of water system 1 were identified. The control system was unreliable and did not activate the water pump consistently. The fluoride pump performed four times faster than expected and, because of improper electrical wiring, could be activated independently of the water pump. Because of these defects, the fluoride concentration of a full holding tank could be increased from 0 to 150 mg per liter in 26 hours. Finally, under certain operating conditions, the fluoride concentrate (18,000 mg per liter) could be siphoned into the well if the hose was kept connected to the drop pipe (Fig. 2) and its free end was placed in the fluoride vat. After the outbreak, tests demonstrated that siphonage could have led to the elevated fluoride concentration by emptying a full fluoride vat in several minutes.

Dose Estimates

Among 62 case patients able to remember how much water they had consumed from water system 1 from May 21 to 23, reports ranged from 2 to 140 ml per kilogram of body weight (median, 27). Assuming that the fluoride concentration of all water collected from May 21 to 23 was 150 mg per liter, the fluoride doses ranged from 0.3 to 21.0 mg per kilogram; 21 persons received an estimated dose of less than 2.0 mg per kilogram, and 10 received doses below 1.0 mg per kilogram. The man who died received an estimated dose of 17.9 mg per kilogram. The estimated fluoride dose strongly correlated with the urinary ($r = 0.78$, $P<0.001$) and serum ($r = 0.71$, $P<0.001$) fluoride

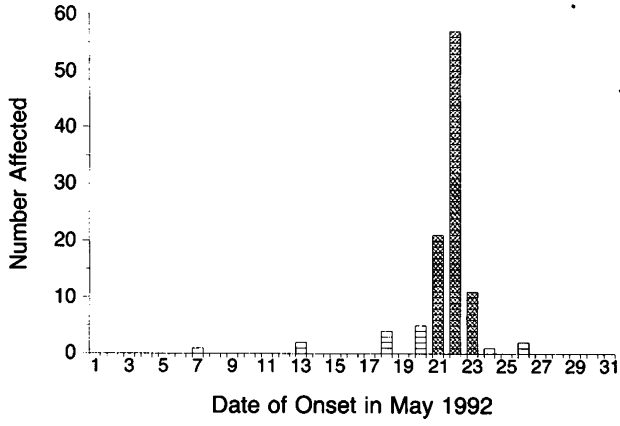

Figure 1. Onset of Symptoms of Acute Fluoride Poisoning in 89 Case Patients and Onset of Gastrointestinal Symptoms in 15 Other Residents of Hooper Bay, Alaska, in May 1992.

Each cross-hatched box denotes one case patient. The open boxes denote residents who had gastrointestinal symptoms before May 21 or after May 23. The date of the onset of symptoms was unknown for two case patients.

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Table 2. Odds Ratios for Various Types of Exposure in a Case–Control Study of Acute Fluoride Poisoning.*

Type of Exposure	Case Patients	Controls	Odds Ratio (95% CI)†
	no. exposed/total no. (%)		
Lived in section 1	39/42 (93)	35/54 (65)	7.1 (1.7–33.4)
Drank water from water system 1	40/42 (95)	26/50 (52)	18.5 (3.7–125.4)
Drank water obtained from water system 1 on May 21, 22, or 23	33/38 (87)	4/50 (8)	75.9 (16.1–419.1)

*Four case patients were included in both the case–control study and the retrospective cohort study.

†CI denotes confidence interval.

Table 3. Attack Rates and Relative Risks for Various Types of Exposure in a Retrospective Cohort Study of Acute Fluoride Poisoning.

Group Examined	No. of Residents	No. of Case Patients	Attack Rate	Relative Risk (95% CI)*
All residents surveyed				
Section 1 residents	81	51	0.63	29.6 (7.4–117.8)
Section 2 residents	94	2	0.02	—
Section 1 residents only				
Usually drank water from system 1	70	50	0.71	7.9 (1.2–51.2)
Usually did not drink water from system 1	11	1	0.09	—
Section 1 residents who usually drank water from system 1†				
Drank water obtained from system 1 on May 21, 22, or 23	47	43	0.91	3.2 (1.6–6.3)
Did not drink water obtained from system 1 on May 21, 22, or 23	21	6	0.29	—

*CI denotes confidence interval.

†Data on two residents and one case patient were missing.

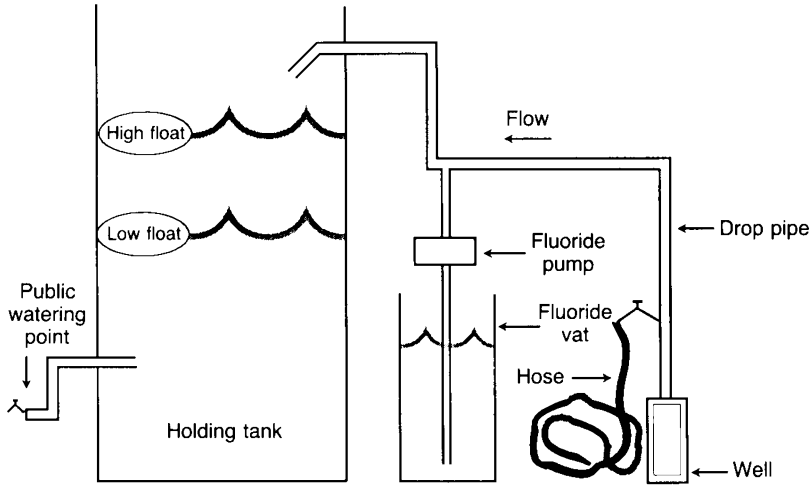

Figure 2. Diagram of Water System 1.

The water pump, the chlorine vat and pump, and the electrical control system are not shown. The water pump was located in the well approximately 23 m (75 ft) underground. The chlorine vat and pump were adjacent to the fluoride vat and pump. The electrical control system connected the high and low floats to the water, chlorine, and fluoride pumps.

concentrations obtained on May 27 or 28 and with the duration of illness ($r = 0.58$, $P<0.001$).

Discussion

These results indicate that excess fluoride entered a community water system in a rural Alaska village, causing 1 death and almost 300 nonfatal cases of fluoride intoxication. The symptoms can be explained by well-described mechanisms.[15] Fluoride and hydrogen ions combine in the stomach to form hydrofluoric acid, which causes nausea, vomiting, diarrhea, and abdominal pain. Fluoride has a direct toxic effect on intracellular metabolism that includes the inhibition of glycolytic enzymes and cholinesterases. Profound hyperkalemia may result. Finally, fluoride forms a complex with calcium in extracellular fluid that causes hypocalcemia; the fate of the complex is not known. Our findings suggest that serum magnesium concentrations may also be reduced; the mechanism for this reduction is unknown. Death from fluoride poisoning is believed to occur from cardiac dysrhythmias due to hyperkalemia or hypocalcemia.[16-18]

Although the interval between water consumption and the onset of symptoms was consistent with that in other reports,[7,19,20] the median duration of symptoms — 24 hours — was longer than the previously reported range of less than 1 hour to 5.5 hours.[9,10,19] The prolonged elevation of serum and urinary fluoride concentrations was also unexpected; more than two weeks after the outbreak, the median serum fluoride concentration among the case patients who were retested was two to three times normal. The half-life of fluoride in serum has been estimated to be 2.4 to 4.3 hours,[21] and after the ingestion of a low dose, the serum fluoride concentration usually returns to normal within 24 hours.[22] The prolonged elevation of serum and urinary fluoride concentrations may have been due to the continued ingestion of water with a high fluoride concentration. This explanation is unlikely, since water system 1 was shut off immediately after the outbreak was recognized, most residents discarded all water obtained from the system, and fluoridation of water system 2 was discontinued. Renal disease and exercise are associated with decreased fluoride excretion, thus lengthening the time that serum fluoride concentrations remain elevated.[15] However, only one person reported having renal disease, none used nephrotoxic drugs, and there is no reason to suspect that the case patients differed substantially from the control subjects with respect to other factors.

The lowest estimated dose of flu-

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oride that caused symptoms was 0.3 mg per kilogram; 16 percent of the case patients received an estimated dose of less than 1.0 mg per kilogram. The lowest level at which an effect was observed — a level of less than 1 mg of fluoride per kilogram — is similar to that reported in some studies,[19,23] but lower than that identified in one report.[24] Disordered mineral homeostasis and cellular damage, including abnormalities in serum magnesium, phosphorus, and lactate dehydrogenase concentrations, persisted for at least 19 days. These effects suggest that both follow-up of individual patients and studies of the long-term effects of acute fluoride poisoning may be indicated.

The correlations of the estimated dose of fluoride with the duration of symptoms and with urinary and serum fluoride concentrations imply that our dose estimates are valid. We made several assumptions, however, and the findings must therefore be cautiously interpreted. We relied on interviews conducted with residents four to five days after the outbreak and did not include water consumed in food in our estimate of the fluoride dose. Although the fluoride concentration in the water system was probably not constant, we assumed that the outbreak was caused by water with a fluoride concentration of 150 mg per liter. Finally, most case patients vomited within minutes after ingesting water with a high fluoride concentration, and the dose estimates did not account for the fluoride lost in this way.

We identified two possible causes of the outbreak. The fluoride pump could have been activated without activation of the water pump, or the fluoride concentrate could have been siphoned into the well. In addition, a series of human errors contributed to this incident. The water-system operator had no formal training and lacked a basic understanding of the operation of the fluoridation unit. Fluoride-test results had not been submitted to or monitored by state regulators. When elevated fluoride concentrations were discovered before the outbreak, the recommendation to disconnect the fluoride pump was not implemented.

The findings of our investigation should be of concern both to health care providers of patients with acute fluoride poisoning and to public health and other officials responsible for water fluoridation. The efficacy of fluoridation in preventing dental caries has been well documented, and the safety of this practice is supported by the extreme rarity of incidents of overfluoridation. We believe that the practice of fluoridation of public water systems should continue. However, public health officials must make certain that standard safety equipment is installed, that water-system operators are properly trained, and that routine, systematic monitoring and follow-up of fluoride concentrations in water systems and inspection of fluoridation units are undertaken.

We are indebted to Mr. Dana Baer, James Bawden, D.D.S., Ph.D., Kim Cowles, D.D.S., Mr. Duane Fridley, Mr. Michael Lewis, John Liddle, Ph.D., Mindy Schloss, M.P.H., Thomas Sinks, Ph.D., Ms. Regina Smith, Robert Quick, M.D., Mr. Art Ronimus, and Mr. Steve Weaver for their contributions to this investigation.

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