Elevated Incidence of Childhood Leukemia in Woburn, Massachusetts: NIEHS Superfund Basic Research Program Searches for Causes

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Between 1966 and 1986, the childhood leukemia rate in Woburn, Massachusetts, was 4-fold higher than the national average. A multidisciplinary research team from MIT, which is being supported by the NIEHS Superfund Basic Research Program, has explored the possible importance of a temporal correlation between the period of elevated leukemia and a previously unrecognized mobilization of toxic metals from a waste disposal site in north Woburn. Residents of Woburn may have been exposed to arsenic (70 µg/l) and chromium (240 µg/l) at levels in excess of federal drinking water standards (50 µg/l for each metal) by consuming municipal groundwater contaminated with these metals. Research is currently underway *a*) to elucidate the mechanisms and the pathways by which these metals were transported from the waste disposal site to the drinking water supply; *b*) to determine the identity of the principal human cell mutagens in samples of aquifer materials collected from the site of the municipal supply wells; and *c*) to measure the extent of exposure and genetic change in residents who consumed the contaminated well water. — Environ Health Perspect 103(Suppl 6):93–98 (1995)

Key words: childhood leukemia; chromium(VI); hazardous waste; Aberjona River; Woburn, MA

Introduction

To better understand the relationships between chemicals in the environment and genetic diseases in humans, toxicologists, analytical chemists, and environmental engineers at Massachusetts Institute of Technology (MIT) have undertaken a study of the presence, movement, and historical use of organic and inorganic toxins in the Aberjona River basin in eastern Massachusetts (Figure 1). This watershed, which contains two U.S. Environmental Protection Agency (U.S. EPA) Superfund sites and over 20 state-identified hazardous waste sites, is home to the Woburn neighborhood, infamous for what the federal Centers for Disease Control called "the most persistent leukemia cluster in the United States" (*1*). From 1966 to 1986, 28 cases of childhood leukemia were reported in Woburn, while only six cases were expected (Figure 2). MIT's multidisciplinary collaboration, which is being funded by the National Institute of Environmental Health Sciences' Superfund Basic Research Program, has considered the correlation between the timing of use of certain municipal drinking water wells, the period of heightened leukemia incidence, and a previously unrecognized major mobilization of toxic metals from waste disposal sites upstream of the wells' water supply. Our goal now is to join with members of the community to test this hypothesis by searching for evidence of actual human exposure.

Background

The upper reaches of the Aberjona watershed have long been home to a variety of industries which have used and/or produced chemicals known to cause mutations (mutagens), cancer (carcinogens), and birth defects (teratogens). Machine degreasers, dry cleaners, and manufacturers have used chlorinated and aromatic solvents; tanneries used chromium as a tanning agent; pesticide manufacturers produced lead arsenate; and sulfuric acid production generated large quantities of arsenic-laden wastes. We have detected high levels of some of these substances in the sediments of streams and ponds on the watershed. The distributions of arsenic and chromium in surface sediments are shown in Figures 3 and 4, respectively. An example of the distribution of organic chemicals in the basin is given for polycyclic aromatic hydrocarbons in Table 1. Using human cell mutation assays, we have found that as much as half the mutagenicity in organic extracts of pond sediments is due to benzo[*a*]pyrene (*3*), a ubiquitous combustion product which has been known since the earliest days of chemical carcinogenesis research to be a potent animal carcinogen.

To reconstruct the time of release of these organic and inorganic chemicals on the watershed, we have dated and analyzed sediment cores from lakes and ponds. In the Upper Mystic Lake—the body of water into which all surface waters of the watershed drain—the deposition rates of benzo[*a*]pyrene and other polycyclic aromatic hydrocarbons (PAH) were found to correlate well with the rates of coal burning (Figure 5). Deposition rates dropped off after the 1940s as coal was replaced by oil and natural gas for home heating. In contrast, when cores were analyzed for toxic metals, a different picture emerged. As seen in Figures 6 and 7, large quantities of arsenic and chromium were deposited in sediments between about 1920 and 1930. The source of these metals appears to be the Industri-Plex Superfund Site, which lies at the headwaters of the Aberjona River (Figure 1) and contains hundreds of metric tons of both arsenic and chromium (*5,6*). Over the years tens of tons of these and other toxic elements have been transported by the Aberjona River to the sediments of the Mystic Lakes (*7*). A second metals

This paper was presented at the Symposium on Preventing Child Exposures to Environmental Hazards: Research and Policy Issues held 18–19 March 1994 in Washington, DC. Manuscript received: December 5, 1994; accepted: May 15, 1995.

This research was supported by NIEHS Superfund Basic Research Program grant 1-P42-ESO4675 and the MIT Center for Environmental Health Sciences grant 2-P30-ESO2109.

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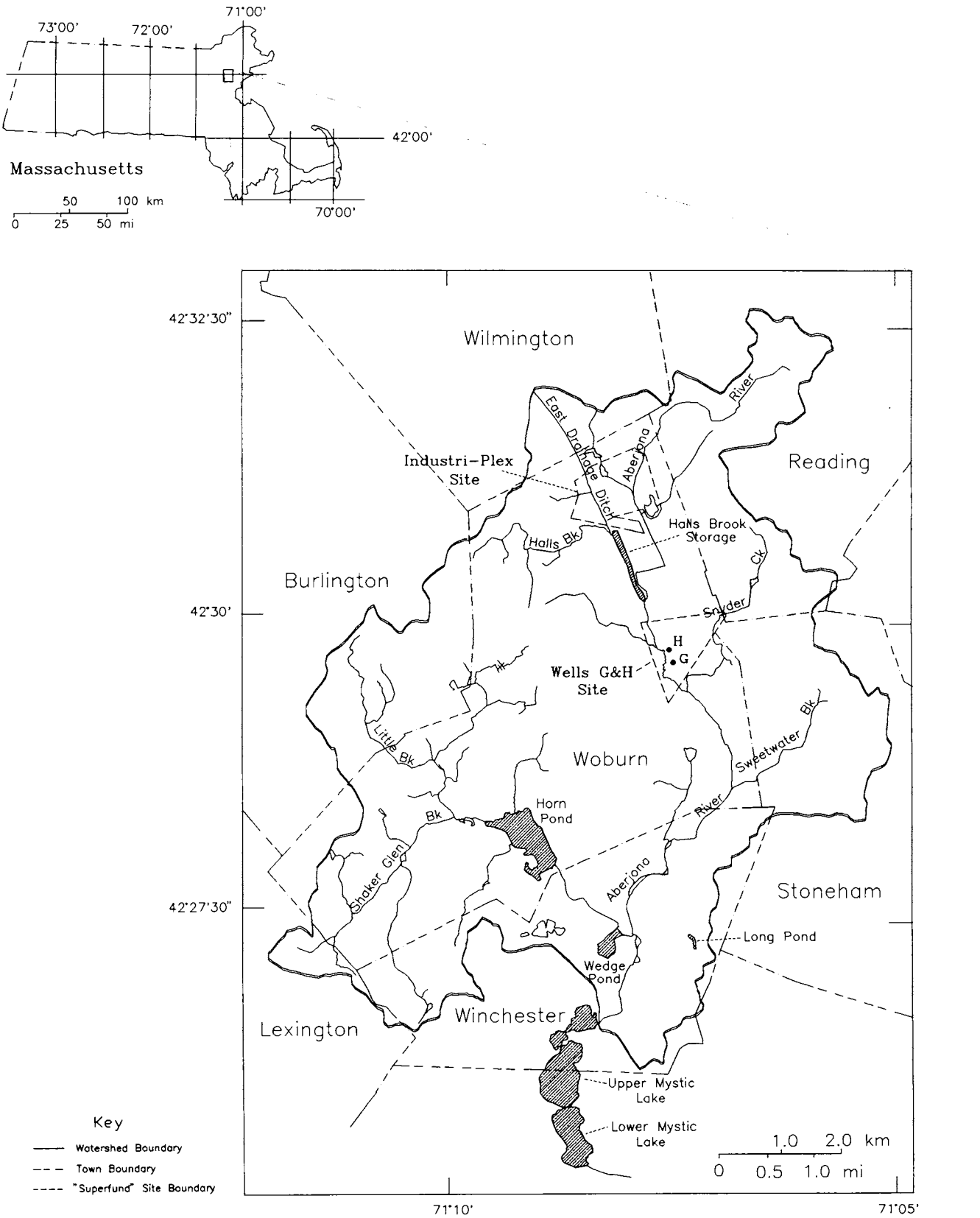

Figure 1. Aberjona watershed.

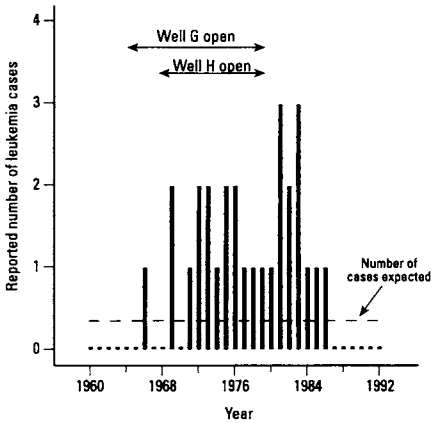

Figure 2. Incidence of childhood leukemia cases in Woburn, Massachusetts, between 1960 and 1992. The expected number of cases in Woburn (population approximately 36,000) for persons 0 to 19 years of age was 0.3 per year (*2*).

mobilization episode, which occurred in the 1960s, appears to have been caused by earth-moving activities aimed at reclaiming the Industri-Plex site for commercial use. Figure 8 is a photograph of this area from 1921 showing one of the "lagoons" used to hold industrial wastewater.

Exposure Pathways

Although a relationship between land redevelopment at the Industri-Plex site, toxic metals deposition in sediments, and childhood leukemia was suggested by these facts, there was no evidence linking the contaminated river water to children living in Woburn. As it meanders through Woburn, the Aberjona River cuts through tracts of commercial and industrial land and several large wetland areas. Since these places typically were not used for recreational activities, Woburn residents would have received little direct exposure to the Aberjona River and its contaminated sediments. However, exposure to Aberjona River water may have occurred after the mid-1960s when two municipal drinking water wells, G and H, were drilled in a wetland area adjacent to the river. The wells were brought on line to supplement water supplies during summer months when water demand was highest. Although residents immediately complained about the foul odor of the water and its brown color, the wells were used until 1979 when chlorinated solvents, including chloroform, trichloroethene, and tetrachloroethene, were detected in well-water samples at levels above federally mandated limits. The area surrounding the wells was subsequently found to be widely contaminated with solvents, pesticides, plasticizers, and toxic metals. As a result, in 1980 the "Wells G and H Site" was added to the National Priorities List of sites eligible for remediation under Superfund. When high numbers of childhood leukemia cases were reported in Woburn between the mid-1970s and early 1980s, the contaminated well water was blamed and the immediate assumption of cause and effect resulted in a series of lawsuits and a widely publicized trial.

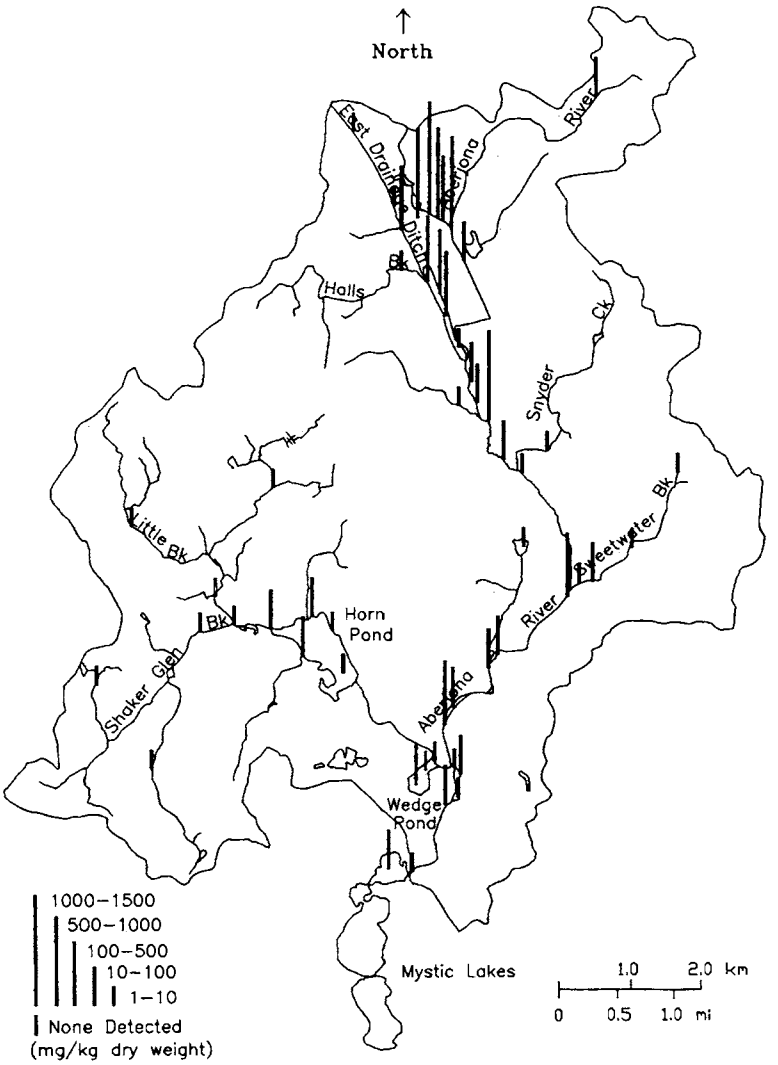

Figure 3. Distribution of arsenic in surface sediments in the Aberjona watershed.

Chemicals of Concern

Although organic solvents were identified as the most hazardous pollutants in the water samples collected from wells G and H in 1979, the abundance of toxic metals at waste disposal sites near the Aberjona River and findings of high levels of metals in river water and sediments raised concerns that toxic metals may also have been present in the well water. Interestingly, wells G and H water samples collected in 1979 did not contain elevated concentrations of toxic metals (*9*). However, in reviewing data from a pump test performed in 1986 (*10*), it has become evident that the aquifer from which wells G and H drew water and the river were hydraulically connected and that during the operation of these wells—between 1964 and 1979—as much as 60% of the water supplying the wells came from the Aberjona River as induced inflow. This means that chemicals in river water could also have infiltrated the aquifer and reached

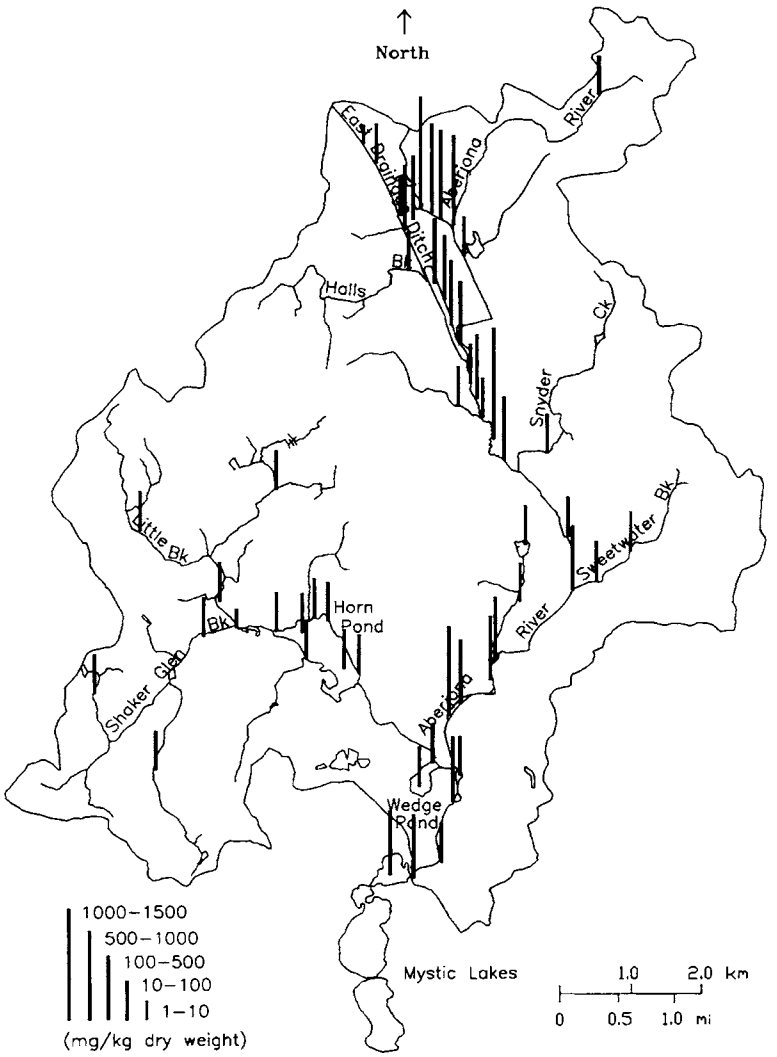

Figure 4. Distribution of chromium in surface sediments in the Aberjona watershed.

Table 1. Concentrations of polycyclic aromatic hydrocarbons in Aberjona watershed surface sediments.[a]

Compound	Upper Mystic Lake, µg/g	Wedge Pond, µg/g	Long Pond, µg/g
Phenanthrene	9.3	5.5	0.9
Anthracene	0.7	0.5	0.05
Fluoranthene	12.4	9.3	1.2
Pyrene	14.2	9.5	1.2
Benz[*a*]anthracene	5.4	4.5	0.3
Chrysene	7.6	5.4	0.3
Benzo[*b*]fluoranthene/ perylene	9.8	7.1	0.8[b]
Benzo[*k*]fluoranthene	3.7	3.1	<0.1
Benzo[*e*]pyrene	8.9	5.9	0.4
Benzo[*a*]pyrene	7.5	5.4	0.5
Benzo[*ghi*]perylene	4.8	3.4	0.4
Indeno[123-*cd*]pyrene	7.7	5.7	0.6

[a]Concentrations are expressed in µg/g dry weight; relative standard deviation ≤10%, $n = 3$. [b]Perylene only.

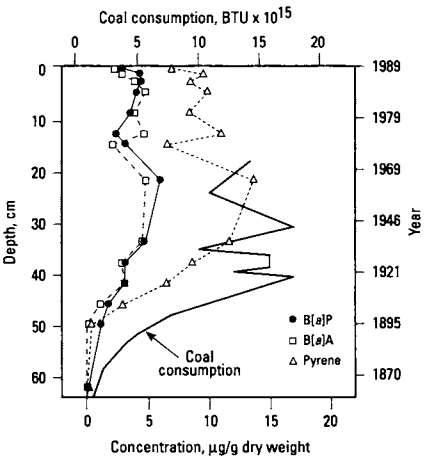

Figure 5. Profiles for selected PAH in a sediment core from Upper Mystic Lake (JM MacFarlane and PM Gschwend, unpublished data). Coal consumption data for the United States is from Hottle and Howard (*4*).

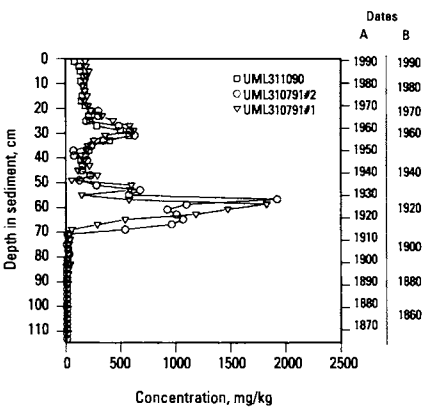

Figure 6. Profiles for arsenic in Upper Mystic Lake from three sediment cores (*7*).

the wells The spatial relationship between wells G and H, the Aberjona River, and the wetland is illustrated in Figure 9.

To learn more about the transport pathways linking the Aberjona River to the wells, we have begun a hydraulic investigation of the wetland in the vicinity of wells G and H. We are also studying sorptive properties of peat material to determine the extent to which metals in recharging river water may have been retarded by the peat and thereby removed from the passing water. When our hydraulic and chemical transport studies are complete, we expect to generate estimates of the amounts of toxic metals that would have been present in well water while the wells were in use. To date our study of peat cores has shown that huge quantities of toxic metals (g/kg amounts) were deposited in the wetland. Using data collected by H Solo (unpublished) we estimate that between the early 1960s and the 1970s on the order of hundreds of µg/l of chromium and arsenic may have been mobilized in the river water passing the wells G and H area.

An additional source of chemicals to wells G and H was the wetland material itself. In hindsight it may have been organic material from the wetland, which was carried by water flowing into the wells, that offended the local residents when the wells were first used. To determine whether mutagenic substances are present in the wetland, we are now testing extracts of peat samples for mutagenicity in human cells. If the peat samples are mutagenic, we will use mutagenicity assay-directed chemcial analysis methods to identify the principal human cell mutagens.

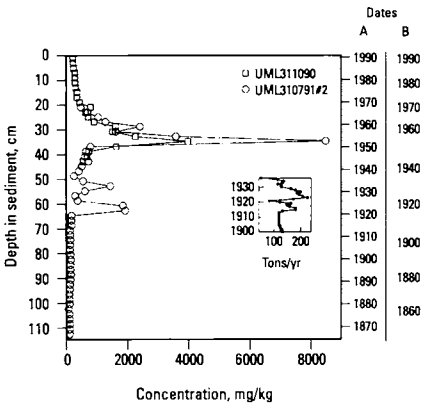

Figure 7. Profiles for chromium in Upper Mystic Lake from two sediment cores. The insert shows the estimated temporal variation of chromium in wastewater discharged by tanneries operating on the watershed (*7*).

Figure 8. Discharge of wastewater from the Merrimac Chemical Company (*8*).

Measurement of Human Exposure

What will toxicologists do with this information? The data in hand suggest that public exposure occurred from drinking water possibly containing 70 µg/l of arsenic and 240 µg/l of chromium (the federal drinking water quality standard for both arsenic and chromium is 50 µg/l). Since ingested arsenic tends to accumulate in hair, analysis for arsenic in hair growing during the period that wells G and H were being used (1964–1979) should help determine whether exposure occurred. We are in the process of obtaining such samples. If the hair analyses indicate that Woburn children were exposed to high concentrations of arsenic and/or chromium, we will use neutron activation analysis for the set of all metals (except lead) that may have been incorporated in teeth and bones growing during the period of confirmed arsenic solidus chromium exposure.

Although these measurements may tell us whether Woburn residents were exposed to high concentrations of toxic metals, demonstration of exposure is not demonstration of cause and effect. In terms of scientific proof, the evidence linking metal exposure—if indeed we do find such evidence—to leukemogenesis would be speculative. Furthermore, by simply analyzing hair samples for the presence of a suite of metals, we would not learn which metal(s), if any, actually caused the biological damage. To deal with this central issue we will use the newly developed technology mutational spectrometry, which allows elucidation of the location, frequency, and nature of mutations in the genetic code. It has been demonstrated that if exposure to a chemical or radiation mutates human cells, mutations are not caused in a random way. On the contrary, a very reproducible and idiosyncratic set of mutations is induced along any DNA sequence by any particular mutagen. Figure 10 shows how the sets of the mutations produced by different mutagens, including chromate, are distributed along a piece of the human X chromosome.

We have devised methods to measure mutations such as those that chromate causes in human cell cultures and human tissue and blood samples. Based on experiments involving very low dose rates in human cell mutation assays and the data of Figure 11, we estimate that the concentration of chromate (as $K_2Cr_2O_7$) necessary to double the rate of mutation in human cells would be about 1 µg/l. This means that a 15-kg child ingesting one liter of water with a total chromium content of 240 µg/l would have an internal concentration of 16 µg/l, an amount which, if present as chromate, is considerably greater than that needed to double the mutation rate. These numbers suggest that continuous exposure over several years to chromium in the water supply could have made chromium mutagenesis a dominant pathway of genetic change in exposed persons. If this is true, we should still be able to find evidence of that exposure

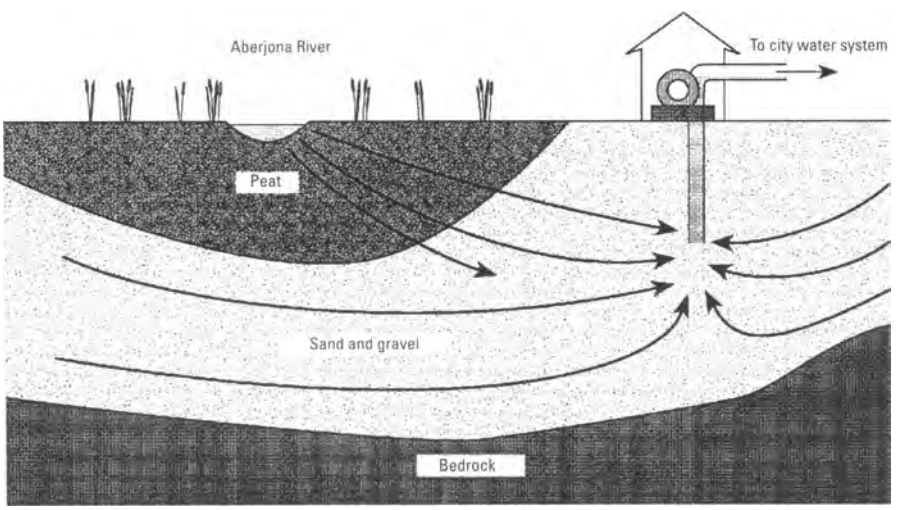

Figure 9. Possible pathways of recharge from the Aberjona River to the sand and gravel aquifer and municipal wells G and H.

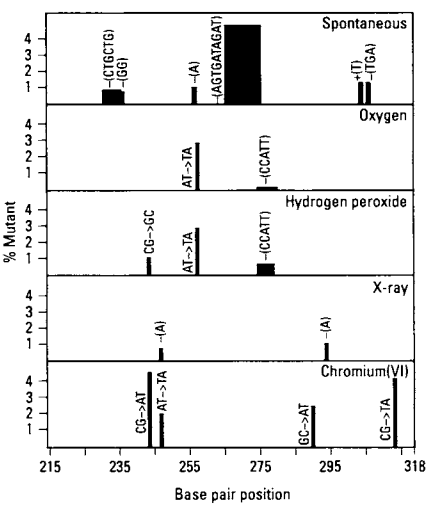

Figure 10. Kinds, positions, and frequencies of 6TG^r mutations induced by $K_2Cr_2O_7$, O_2, H_2O_2, X-rays in the low melting domain of exon 3 on the *hgprt* gene in human lymphoblastoid B-cells (TK6) (*10*).

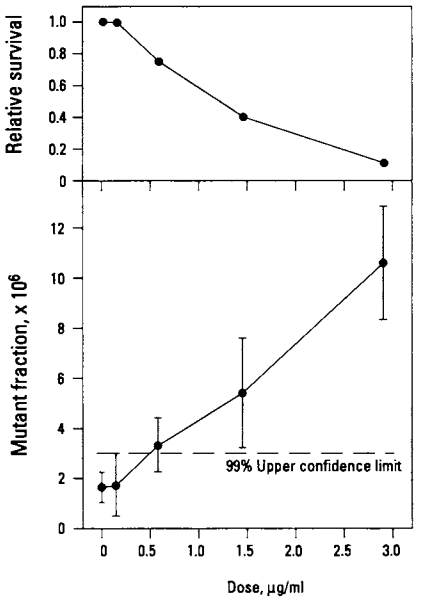

Figure 11. Mutagenicity and toxicity induced in human lymphoblastoid B-cells (TK6) by 5-hr exposure to $K_2Cr_2O_7$. Each response represents the mean of three independent cultures. Error bars represent 99% confidence levels (*11*).

in the form of chromium-induced mutations in blood cell samples taken today.

Summary

We are exploring the possibiliy that the elevated levels of childhood leukemia observed in Woburn over the 21-year period between 1966 and 1986 may have been caused by exposure to toxic metals introduced into the city's drinking water supply from contaminated groundwater. To test this hypothesis we are developing new field measurement techniques to determine the pathways by which these metals entered the city's groundwater aquifers, we are testing aquifer materials to determine whether they contain human cell mutagens, and we are collecting hair samples from Woburn residents to analyze the extent of toxic metals exposure. If evidence of exposure is found, we will use mutational spectrometry to measure the patterns of mutations in the DNA of exposed individuals. Mutational spectrometry has not been used in human population studies before; therefore, we have made efforts to establish a dialogue with the community about what we are trying to do and why, and to address concerns raised by community members. We realize that the success of our research depends on the support of Woburn residents, and thus it is incumbent upon us to explain fully the nature of our experimental methods and what the results can and cannot tell us. With community support, the resolving power of mutational spectrometry, and the essential contributions of the analytical chemists, environmental engineers, and other members of our multidisciplinary initiative, we hope to find a cause for the elevated incidence of childhood leukemia in Woburn. In doing so, we further hope our effort will help bring the field of environmental health science to the point where it can provide scientifically sound answers to many other public health questions that we are presently unable to answer.

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