Hexavalent Chromium, Yellow Water, and Cancer
A Convoluted Saga

Allan H. Smith

Abstract: In this issue, Beaumont et al report cancer mortality rates associated with exposure to high concentrations of hexavalent chromium in well water in Liaoning Province, China. Contamination of drinking water at these levels has been reported only once before, among a small group in Mexico. The investigation in China is a convoluted tale. The first report indicated an increase in cancer mortality, while a subsequent publication with the same lead author claimed no increased risks. In 2006, the journal publishing the latter paper retracted it because of failure to disclose financial and intellectual input to the paper by outside parties (linked to chromium polluting industries). Beaumont and his colleagues now provide a further reanalysis of these data, showing increased mortality in particular from stomach cancer, but with serious limitations in the data and methods of analysis. These limitations are counterbalanced by the importance of a study of perhaps the highest exposure to hexavalent chromium in water that will ever be experienced by a population large enough to estimate risks of cancer.

(*Epidemiology* 2008;19: 24–26)

There are 2 places in the world where well water had become so contaminated by hexavalent chromium that the water turned yellow. One is in León, Mexico, near a factory producing chromium compounds for leather tanning.[1] The other is in Liaoning Province, China, near a factory producing ferrochromium for steel production.[2] The latter is the topic of a paper appearing in this issue.[2]

In both countries, contaminated wells were the source of water for household use, including drinking. Inhalation of hexavalent chromium is a known cause of lung cancer,[3] but, as noted by Beaumont et al, animal bioassays have reported that chromium ingestion also causes intestinal tract tumors.[2] This has raised concerns that ingestion of hexavalent chromium may increase the risk of human cancer, in particular gastrointestinal cancer. To generate the best causal evidence, human studies need to be in populations with high exposures, so one might first consider the 2 places in the world where concentrations of hexavalent chromium were high enough to discolor water (above about 0.5 mg/L).[1]

The factory that contaminated the wells in Mexico commenced operations in 1970. This factory is located about 10 km outside of the city of León, in the province of Guanajuato. I recently visited the site of the contaminated wells. The well reported to contain yellow water is now closed, and there are only a few scattered dwellings nearby. Other wells within a kilometer or so of the factory had also been contaminated with hexavalent chromium, although not at concentrations high enough to discolor the water.[1] One contaminated well supplied the small village of Buena Vista, with a population of less than 1000 people. Where the well once stood, there is only a vacant lot by the rough cobbled main street. A small population such as this village, exposed for only a few years, is unlikely to give sufficient statistical power to detect increased risks of cancer of specific sites. In Mexico, mortality rates from stomach cancer are between 5 and 10 per 100,000 person-years.[4] If 1000 people in or near Buena Vista had been exposed and then followed for 10 years, the expected number of deaths from stomach cancer would be less than 1—too few to detect excess risk unless the risk was extremely high.

The population exposed in Liaoning Province, China, was much larger. There were close to 100,000 person-years of mortality follow-up in the exposed villages during 1970–1978 (estimated for villages V–IX, Table 3 of the Beaumont et al paper[2]). This would seem an excellent opportunity, and perhaps the only place in the world, where the effects of ingestion of hexavalent chromium could be studied with adequate power. Around the year 1980, Zhang and Li authored an unpublished report noting increased stomach and lung cancer mortality rates in the exposed villages.[2] The first publication of these results was in 1987 in the *Chinese Journal of Preventive Medicine*.[5] An unfortunate sequence of events followed (Table 1).

In 1997, Zhang and a Chinese colleague published a paper in English, but this time with the conclusion that "the results did not indicate an association of cancer mortality with exposure."[6] Evidence emerged later to suggest that this paper was really the work of a US consulting firm, ChemRisk,

Submitted 14 September 2007; accepted 25 September 2007.
From the School of Public Health, University of California, Berkeley, California.
Supported by NIEHS grant P42 ES04705, and from the Center for Occupational and Environmental Health, University of California, Berkeley.
Correspondence: Allan H. Smith, School of Public Health, University of California, Berkeley, CA 94720. E-mail: ahsmith@berkeley.edu.

ISSN: 1044-3983/08/1901-0024
DOI: 10.1097/EDE.0b013e31815c40dc

TABLE 1. Chronology of Key Events Concerning Contamination of Wells With Hexavalent Chromium and Subsequent Reports Concerning Cancer Mortality in Exposed Populations in Liaoning Province, China

1959	Production of ferrochromium commenced in a factory in Liaoning Province, China.
1964	Residents living near the factory report yellow color in nearby wells used for drinking water.
1965	Documentation of high levels of hexavalent chromium in local wells; beginning of remediation efforts.
1967	Documented declines in concentrations of chromium in groundwater.
1987	Publication by Zhang and Li in the *Chinese Journal of Preventive Medicine* reporting increased stomach and lung cancer mortality for the period 1970–1978 in the population living near the factory.[5]
1997	Publication apparently by Zhang and Li in *J Occup Environ Med* (JOEM) of a "clarification and further analysis" stating that the "results do not indicate an association of cancer mortality with exposure."[6]
1999	Death of Zhang.
2006	Editor of JOEM retracts the 1997 article by Zhang and Li because "financial and intellectual input to the paper by outside parties was not disclosed."[7]
2007	Beaumont et al report a stomach cancer mortality rate ratio of 1.82 (95% CI = 1.11–2.91) for exposed compared with unexposed villages.[2]

which had been hired by industry clients with liability for chromium pollution in the United States.[7] In 2006, the editors of the *Journal of Occupational and Environmental Medicine* retracted the paper, stating that "financial and intellectual input to the paper by outside parties was not disclosed."[8] The study by Beaumont et al published in this issue[2] reexamines the same study population, and concludes there was an increased rate of stomach cancer in the exposed villages compared with unexposed villages (rate ratio = 1.82; 95% confidence interval 1.11–2.91). However, the authors note limitations in their data and methods of analysis.

Indeed, there are serious limitations. The study involves a rather messy reanalysis of mortality for the period 1970–1978—the same data on which the previous 2 publications were based. In 1979, the investigators in China had obtained death records and calculated mortality rates. Dr. Zhang has since died. Beaumont and his colleagues cannot even reconstruct how the place of residence at the time of death had been determined. They give 3 possibilities: the place of residence was based on the death certificate information, on the village where the death certificate was filed, or on information from survivors.

Only crude rates were available for stomach and lung cancer from any village. Data on stomach cancer were unavailable for one of the villages, and data on lung cancer were unavailable for another. To make matters worse, mortality rates were not available by individual years; data had been combined for the period 1970–1978, so any trends over time (perhaps related to latency) could not be examined. Beaumont et al did what might be described as a rough age adjustment based on the known impact of age adjustment on the combined all-cancer crude mortality rates. There were also no sex-specific data, with mortality for men and women having been combined in the available data. This is surely an epidemiologist's ultimate nightmare, being unable to adjust properly even for age and sex.

Yet epidemiology is often at its best when functioning as an opportunistic observational science. Better to conduct shoddy studies of high exposures than high-quality studies of low exposures. It is a bit like the man who searched for his lost wallet under a lamppost. When asked where he lost it, he points to an area in the dark—but, he says, "the light is better over here." Epidemiologic studies are too often conducted where it is easy to do them, rather than where the real evidence may be found. The excuse is that the high exposures occur where studies are difficult to conduct. Indeed, the future of environmental epidemiology lies in the developing world, where studies are usually difficult to do.

I commend Beaumont and his colleagues for struggling with an epidemiologic analysis with poor data. If there are human risks from hexavalent chromium in water, such risks are more likely to be found where exposures are high than by insisting on high-quality studies of populations where exposures are much lower.

Does the Beaumont reanalysis prove that ingestion of chromium causes cancer in humans? Of course not. Does it provide evidence that is consistent with there being increased risks? I suggest it does. Perhaps the greatest weakness of the evidence is the very short latency from exposure to increased mortality risks. Even if the exposures started as early as 1960, the latency for the period 1970–1978 reported here involves just 10 to 18 years, which (as noted by the authors) is very short for solid tumors. One would hope for and urge further follow-up of this exposed population in China, including both mortality studies and perhaps also case-control studies of stomach cancer. There may be no other population in the world that can provide such valuable information concerning ingestion of hexavalent chromium in water and human cancer.

ACKNOWLEDGMENTS

I gratefully acknowledge the assistance of Ayse Ercumen and Jane Liaw.

ABOUT THE AUTHOR

ALLAN SMITH has been a Professor of Epidemiology at the University of California, Berkeley School of Public Health since 1983. In recent years his research has focused on cancer and other health effects of arsenic in drinking water, with studies of exposed populations in Argentina, Chile, Bangladesh, and India.

REFERENCES

1. Armienta-Hernandez MA, Rodriguez-Castillo R. Environmental exposure to chromium compounds in the valley of Leon, Mexico. *Environ Health Perspect*. 1995;103(suppl 1):47–51.
2. Beaumont JJ, Sedman RM, Reynolds SD, et al. Cancer Mortality in a Chinese population exposed to hexavalent chromium in drinking water. *Epidemiology*. 2008;19:12–23.
3. International Agency for Research on Cancer (IARC). Chromium and chromium compounds. In: *IARC Monographs on the Evaluation of Carcinogenic Risks in Humans: Chromium, Nickel, and Welding*. Lyon: 1990;49.
4. Tovar-Guzman V, Hernandez-Giron C, Barquera S, et al. Epidemiologic panorama of stomach cancer mortality in Mexico. *Arch Med Res*. 2001; 32:312–317.
5. Zhang JD, Li XL. [Chromium pollution of soil and water in Jinzhou.] *Zhonghua Yu Fang Yi Xue Za Zhi*. 1987;21:262–264.
6. Zhang JD, Li S. Cancer mortality in a Chinese population exposed to hexavalent chromium in water. *J Occup Environ Med*. 1997;39:315–9.
7. Egilman D, Scout. Corporate corruption of science–the case of chromium(VI). *Int J Occup Environ Health.* 2006;12:169-176.
8. Brandt-Rauf P. Editorial retraction. *J Occup Environ Med*. 2006;48: 749.