We read with interest the article by Sheppard et al. (2006) on elevated W and Co in airborne particulates in Fallon, Nevada and the possible implications for the high incidence of childhood leukemia that has occurred in Fallon. While the reported findings are of great interest, we are concerned about the study design and the interpretation of the data presented in this paper. In addition, we are also concerned by the conclusion that elevated airborne concentrations of W and Co in the air of Fallon, Nevada are associated with a specific industry, and the suggestion that they are somehow related to the Fallon childhood leukemia cluster.

Sheppard et al. (2006) present information regarding methods used to collect and analyze dust samples from five cities in western Nevada using high volume air samplers. Median W and Co loading values are reported in units of ng/m³ for each of the sampling sessions. However, total dust concentrations and concentrations of these elements in dust samples and in blank samples were not reported. Method detection limits and method accuracy and precision also were not reported. Because these data were not provided, the reader cannot assess the underlying reliability and significance of the data presented. For example, the reader cannot determine whether the concentrations of W and Co in Fallon dust are similar to concentrations of W and Co in dust collected from the other cities. Similarly, one cannot determine whether the differences in W and Co loadings between Fallon and the other cities are associated with differences in W and Co concentrations in dust, or due to the differences in loading associated with differences in concentrations of dust in the air. Finally, data are not presented to determine whether sampling locations within Fallon with elevated W and Co also have elevated total dust concentrations.

Sheppard et al. (2006) state that wind speeds “play a role in controlling metal loading and dust”. We disagree with the interpretations of the data presented. For example, Fig. 4 illustrates the relationship between the median W loading and wind speed for Fallon samples collected during the March and November 2004 sampling sessions. Separate regressions were developed for the March and November data, and the authors provide no reason for separating these data in the analysis. If taken together, the data show no relationship ($R^2 > 0.1$) between median W loading and wind velocity.
Likewise, for the November regression, the $R^2$ shown was calculated excluding “the high outlying value”. However no attempt was made to explain the reason for excluding this value, and no statistical analysis was provided to demonstrate this value should be considered an outlier.

Sheppard et al. (2006) are inconsistent in their data interpretations. The median W loading of 0.57 ng/m$^3$ for the March Fallon-Yerington sampling session was described as an “anomalously low metal loading.” However, this median W loading of 0.57 ng/m$^3$ was greater than the median W loading for the March Fallon-Lovelock sampling session described as an “anomalously low metal loading.” However, this median W loading of 0.57 ng/m$^3$ was greater than the median W loading of 0.10 ng/m$^3$ recorded for the November Fallon-Lovelock sampling session. The authors contend that “the session with anomalously low metal loadings had strong winds [average wind speed of 6.1 m/s] that were predominantly northerlies… possibly indicating a wind direction and/or speed effect on metal loading in dust of Fallon.” However, for the November session with the lower median W loading, the average wind speed was lower (2.1 m/s) and winds were from a different direction (SE). These latter findings contradict the claim that the “anomalously low” loading was correlated with wind speed and direction.

Sheppard et al. (2006) contend that W loadings in Fallon dust vary as a function of distance from a hard-metal facility located within the town of Fallon. Fig. 7 shows W and Co loadings as a function of distance of the sampling location from the hard-metal facility along with $R^2$ values for power function regressions of loading and distance. Two sampling locations were excluded from the regression analyses for W and Co. The authors contend that these two sampling locations underfit the relationship because the sampling locations are SW, or predominantly upwind, of the hard-metal facility. Based on the wind rose provided in Fig. 3(b), approximately 40% of winds were from the north and NNE during this sampling event, placing these southwesterly locations downwind of the hard-metal facility for a substantial portion of the sampling event. It would be helpful if the authors provided a map showing sampling locations in relation to the hard-metal facility and also explain why 60% of the sampling locations are located within ~2.3 km of the hard-metal facility. Clustering these sampling locations so close to the facility suggests a priori sampling bias towards the facility.

Sheppard et al. (2006) incorrectly characterize “typical atmospheric loading” of W (0.5–1.0 ng/m$^3$) and Co (1 ng/m$^3$) as “ambient standards.” The use of the term “standard” in this context implies that these values are accepted regulatory limits for ambient air concentrations for these constituents. The American Conference of Governmental Industrial Hygienists (ACGIH) has set threshold limit value (TLV) 8 h time weighted averages (TWA) of 5 mg/m$^3$ (5,000,000 ng/m$^3$) for W (as W) (ACGIH, 2003) and 0.02 mg/m$^3$ (20,000 ng/m$^3$) for Co (ACGIH, 2000). The National Institute for Occupational Safety and Health (NIOSH) has set recommended exposure limits (REL) of 10 h TWA of 5 mg/m$^3$ (5,000,000 ng/m$^3$) for W (NIOSH, 2006a) and 0.05 mg/m$^3$ (50,000 ng/m$^3$) for Co (NIOSH, 2006b). The Occupational Safety and Health Administration (OSHA) has set permissible exposure limits (PEL) 8 h TWA of 5 mg/m$^3$ (5,000,000 ng/m$^3$) for W for shipyard and construction workers (OSHA, 2005a,b) and 0.1 mg/m$^3$ (100,000 ng/m$^3$) for Co (OSHA, 2006). These standards for airborne W and Co are many orders of magnitude greater than the highest ambient concentrations of W and Co measured in air by Sheppard et al. (2006).

The authors suggest that W and Co in airborne particulates in Fallon, Nevada may have possible implications for the high incidence of childhood leukemia in Fallon. The data presented in this article suggest that W loadings rapidly drop off to values that are consistent with “typical ambient loadings” of 10 ng/m$^3$ or less within about 2 km of the hard-metal facility. Based on Fig. 3 of the US Agency for Toxic Substances and Disease Registry (ATSDR) Air exposure pathway assessment: Fallon leukemia project (US ATSDR, 2003), homes of the case families were located outside of the modeled area of impact from emissions from the hard-metal facility. As concluded by the ATSDR report (2003) the locations of the homes with respect to the hard-metal facility is inconsistent with an airborne exposure to emissions from the facility as a cause of the high incidence of leukemia.

The Centers for Disease Control (CDC) conducted a thorough investigation into the Fallon leukemia cases; in fact it was the largest such investigation ever undertaken in the US. The scientists for the CDC and state health department concluded that exposure to W (including airborne W) was not associated with the incidence of childhood leukemia in Fallon (CDC, 2003).

In conclusion, we are concerned that Sheppard et al. (2006) were overly selective in their data.
presentation and were inconsistent in their interpretations and characterizations of the data presented.

References


Comment

Reply to comment on “Elevated tungsten and cobalt in airborne particulates in Fallon, Nevada: Possible implications for the childhood leukemia cluster”, by Blasland, Bouck & Lee, Inc.

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1. Introduction

Several criticisms of Sheppard et al. (2006a) are raised in this comment. One, airborne W and Co loadings are expressed as mass of element per volume of air rather than mass of element per mass of dust and therefore cannot be reasonably interpreted. Two, inter-seasonal patterns of airborne W and Co in Fallon seem inconsistent. Three, the role of wind direction on airborne W and Co in Fallon is not clear. Four, elevated levels of airborne W and Co in Fallon do not approach threshold limits of exposure established for workplaces. Five, children of Fallon do not necessarily live near the hard-metal facility in Fallon and therefore are not exposed to elevated airborne W and Co. Six, research on total suspended particulates of Fallon was not warranted because airborne W in Fallon had been studied already. The authors respond to these criticisms as well as to additional points made in this comment.

2. Units of airborne metal particulates: mass per volume versus mass per mass

The issue of expressing airborne metal particulates in terms of mass of element per volume of air rather than mass of element per mass of dust has been explained in response to an earlier comment (Sheppard et al., 2006b). Without repeating all of that explanation here, the salient points are as follows:

- Using volume of air in the denominator standardizes mass quantities of particulates so that they can be compared through time and space, facilitating inter-town comparisons.
- Using mass of dust in the denominator makes mass per mass a ratio of two environmental variables so that comparisons of mass quantities of particulates through time and space would be ambiguous.
- In scientific literature on airborne metals in total suspended particulates, the dominant unit of expression is mass per volume.
- In research on airborne metals of Fallon, there are no differences in results or interpretations using mass per volume versus mass per mass.

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At the regional scale, airborne W and Co can be elevated in Fallon relative to comparison towns of west central Nevada. At the local scale, airborne W and Co can be elevated in central Fallon relative to the outskirts of Fallon. These results are equally true using either unit.

3. Inter-seasonal analysis of airborne particulates

Total suspended particulates were sampled in two distinct seasons, spring (mid-March through early April) and fall (early November). This strategy was not intended to compare absolute loadings of airborne particulates between seasons. Absolute levels of airborne particulates can vary substantially across seasons due to different weather, including wind, temperature, and precipitation (Wakamatsu et al., 1996; Kim et al., 1997; Pandey et al., 1998; Browne et al., 1999; Querol et al., 1999; Zheng and Fang, 2000). Sure enough, in Fallon the March collection period was windy (average wind speed of 4.5 m s\(^{-1}\)), warm (average temperature of 14 °C), and dry (no rain fell at all during the entire collection period), but the November collection period was relatively calm (average wind speed of 1.8 m s\(^{-1}\)), cool (average temperature of 9 °C), and wet (during the 5-day collection period, 25 mm of rain fell, about one-fifth of the normal annual rainfall for Fallon). Such a large difference in weather rendered inter-seasonal comparisons of absolute values of airborne particulates of little value in this research whose objectives included identifying something distinctive environmentally about Fallon relative to comparison towns of west central Nevada. Comparing a single absolute loading in March with a single absolute loading in November is not valid, nor is analyzing the effects of wind speed on airborne metal loadings at the inter-seasonal scale.

The key advantage of collecting airborne particulates from different seasons is having replication at the project level to test relative patterns of airborne metal loadings under different atmospheric conditions. This advantage proved to be useful. In both seasons, Fallon had significantly higher levels of airborne W and Co relative to comparison towns. In both seasons, airborne W and Co co-varied at the daily or sub-weekly scale. In both seasons, wind speed correlated to at least some degree with airborne W levels. Replication of these relative patterns across two different seasons provides stronger evidence for elevated W and Co being a distinctive environmental feature of Fallon than if these relative patterns had been demonstrated for just one season.

4. The role of wind direction on airborne W and Co in Fallon

If the hard-metal facility in Fallon were assumed to be the source of airborne W and Co in Fallon (which is not to claim that it is, but only to establish a starting point for spatial analysis), there are two outlying data points in the distance decay model for airborne W and Co (Sheppard et al., 2006a, Fig. 7). These two points are explainable based on their locations relative to the facility and wind directions of that sampling session. These two sampling locations are SW of the hard-metal facility, and the predominant directions of strong winds (>4 m s\(^{-1}\)) during that session were from west and/or south (Sheppard et al., 2006a, Fig. 3b). Disregarding calm winds (<4 m s\(^{-1}\)), which accounted for 59% of all winds of that session, 70% of strong winds were from west and/or south. Only 30% (not 40%) of strong winds were from north and/or east. In other words, a clear majority of strong winds during that session were from west and/or south. Thus, the two sampling locations with outlying low W and Co loadings were mostly upwind of the hard-metal facility for that sampling session.

5. Threshold limit values for workplaces

Comparing ambient levels of airborne contaminants with threshold limit values (TLV) set for workplaces is inappropriate. As emphasized by the American Conference of Governmental Industrial Hygienists (ACGIH, 2003, p. 3), TLVs are not to be used “in the evaluation or control of community air pollution nuisances; in estimating the toxic potential of continuous, uninterrupted exposures; or as proof or disproof of an existing disease or physical condition.” Furthermore, “TLVs are not [emphasis of the ACGIH] fine lines between safe and dangerous concentrations, nor are they a relative index of toxicity.” These admonitions against using TLVs as community air standards or as fine lines between safe and dangerous concentrations have been independently confirmed and emphasized (Stokinger, 1969, 1973; Paull, 1984; Alavanja et al., 1990; Hewett, 1996).

The ACGIH also implores that the background documentation (ACGIH, 2001) be considered to
understand how the TLV for any given contaminant is determined (ACGIH, 2003, p. 3). With respect to airborne W and Co in Fallon, the documentation is instructive. For comparison purposes, TLVs for notorious metal contaminants like Hg and Pb are based on extensive documentation, including especially studies with human subjects (Table 1). In sharp contrast to these well-known metal contaminants, the TLV for W is based on relatively little documentation. The TLV for Co is based on more documentation than for W but less than for Hg and Pb. Even if TLVs were appropriate benchmarks for assessing ambient levels of airborne W and Co, which they are not, the relatively sparse documentation for Co and especially for W would have to be taken into account when evaluating their TLVs. Moreover, the TLV for W is currently under review (ACGIH Science Group, personal communication to Sheppard, 2006), and when TLVs are re-evaluated, they are often lowered, sometimes by large factors (Roach and Rappaport, 1990).

6. Children of Fallon do not necessarily live in the area of elevated airborne W and Co

No attempt was made to place air samplers at homes of children with leukemia (Sheppard et al., 2006a, p. 154). Instead, the broader objective was to test more generally throughout Fallon for any contaminant that might be distinctive relative to comparison towns of west central Nevada. This approach eliminated home locations of children with leukemia as a research factor. An obvious question arises: are children of Fallon exposed to elevated airborne W and Co? An important factor in children’s health is their time spent at school, which amounts to a substantial fraction of waking hours on school days (Briggs et al., 2003; Elgethun et al., 2003; Green et al., 2004). Time spent at school, both in class and in recess, can affect children’s exposure to particulate matter (Allen et al., 2004). Accordingly, exposure to airborne particulates is not just a matter of where children live, but also where they go to school. All public schools of Fallon are located within 3 km of the hard-metal facility (Fig. 1), which encompasses the potential extent of elevated airborne W and Co (Sheppard et al., 2006a, Fig. 7 and text on p. 161). Children who attend public school in Fallon spend some amount of time within areas of Fallon that can have elevated airborne W and Co. Once again, this is not to claim that the hard-metal facility is the source of the elevated airborne W and Co in Fallon.

7. Prior CDC research on airborne W in Fallon

Contrary to the comment by Blasland, Bouck & Lee, Inc., the Centers for Disease Control, 2003 report entitled, “Cross-sectional exposure assessment of environmental contaminants in Churchill County, Nevada” (US CDC, 2003), did not demonstrate that exposure to airborne W was not associated with childhood leukemia in Fallon. Agreed, no relation between leukemia and W exposure was stated (US CDC, 2003, p. 14), but this particular finding referred to case-comparison analyses of W.

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Table 1
Number of references cited in the documentation for TLVs of selected metal contaminants for workplace environments (ACGIH, 2001)
in urine samples (US CDC, 2003, Table 3 on p. 26) and did not include environmental exposure data. Also agreed, W had not been previously associated with acute lymphocytic leukemia (US CDC, 2003, p. 19), but this was a broad discussion point referring to the fact that general biomedical research had not yet associated W with leukemia. This discussion point did not include environmental data. Environmental data were analyzed, including air, but strictly speaking, airborne W was not investigated in this report. Air samples of the CDC investigation were “grab” (instantaneous) samples that were analyzed for volatile organic compounds (US CDC, 2003, p. 17 and Appendix E), not for W or other metals.

Furthermore, the CDC grab samples were of indoor air collected from inside homes (US CDC, 2003, p. 9 and Appendix E). The notion that prior research on indoor air obviates additional study of outdoor total suspended particulates is untenable. With respect to air quality, indoor air is profoundly different from outdoor air. Indoor environments have various blocks against infiltration of outdoor air (Brooks and Davis, 1992). Indoor air also has many sources of contamination that are not found outdoors (Li, 1994; Long et al., 2001). Direct comparisons of indoor versus outdoor air show particulate matter generally and airborne metals specifically to be variously elevated indoors (Rasmussen et al., 2001; Jones et al., 2000; Jaradat et al., 2004) or outdoors (Rowe et al., 1985; Madany et al., 1994; Al-Rajhi et al., 1996; Tong, 1998; Shilton et al., 2002; Yiin et al., 2004). Depending on specific circumstances, total suspended particulates and airborne metal concentrations in paired indoor and outdoor settings can correlate significantly (Li, 1994; Wolz et al., 2003) or not at all (Tong, 1998; Jones et al., 2000; Rasmussen et al., 2001). Given this lack of consistent association between air quality indoors versus outdoors, indoor air and outdoor air are considered to be different environments (Allen et al., 2004). Testing outdoor air of Fallon was fully justified, even with prior research on indoor air.

The more pertinent prior research was the outdoor air testing that was reviewed by the US Agency for Toxic Substances and Disease Registry (US ATSDR, 2003). Data generated for that research show airborne Co to be five times higher on average inside Fallon than outside of Fallon (US ATSDR, 2003, Table 6, p. 59). Tungsten was not measured. However, that research used only one air sampler within Fallon and one outside of Fallon, and the ultimate conclusion was no association between air pollutants and leukemia (US ATSDR, 2003, p. 25). Outdoor air sampling was expanded by using 10 high-volume samplers to collect airborne particulates at multiple locations in Fallon and multiple locations in multiple comparison towns (Sheppard et al., 2006a). Then the entire project was repeated during a different time of year using completely different field equipment.

8. Additional responses

Inductively coupled plasma mass spectroscopy is appropriate and effective for measuring metals on air filters. Specifically, minimum detection limits for W were 3–4 orders of magnitude lower than W values measured on filters, and minimum detection limits for Co were 2–3 orders of magnitude lower than Co values measured on filters. Recoveries from certified control material (SRM1648, urban particulate matter) averaged 95% for W and 115% for Co.

The very high W loading value during the November collection period (Sheppard et al., 2006a, Fig. 5a) is obviously an outlier, being 4–400 times higher than other Fallon values of that collection period. In regression tests for the wind speed analysis, that value resulted in a large standardized residual, which justified its exclusion from the regression model (Grubbs, 1969). The question remains: what caused airborne W loadings to be so high for that sampling session? This was not a measuring error for W in particular, as airborne Co loadings for that sampling session were similarly very high (Sheppard et al., 2006a, Fig. 5a). It could be that variability in the source of airborne W and Co in Fallon caused those extraordinary W and Co loadings, but this is not knowable currently, as the source of airborne W and Co in Fallon has not been conclusively identified.

The accusation of bias in sampling is wrong and unfounded. The placement of airborne dust samplers in Fallon was not purposely focused around the hard-metal facility. From prior research, cases of childhood leukemia in Fallon have not been associated with the facility (US ATSDR, 2003, p. 18). Instead of focusing on the hard-metal facility, the strategy for deploying total suspended particulate samplers was to represent each community spatially as best as possible (Sheppard et al., 2006a, p. 154). In Fallon, that meant sampling densely near the center of town, where variability in airborne particulates was assumed to be high, and more sparsely towards the outskirts of town, where variability in
critical evaluation of research is an important element of science. As one form of critical evaluation, comment-reply about an article can serve a useful purpose by clarifying details of published research (Krausman et al., 2003). However, comment-reply does not necessarily constitute follow-up research, such as that which is called for in Fallon. Much research remains to be done in Fallon related to its cluster of childhood leukemia; it is to be hoped that it proceeds in due course.

9. Conclusion

The conclusion of Sheppard et al. (2006a) still stands: Fallon, or more precisely central Fallon, is distinctive environmentally by its elevated airborne W and Co. This conclusion merits follow-up investigation, namely to confirm elevated airborne W and Co, to identify the chemistry and morphology of the W and/or Co particles, and to pinpoint the source of elevated airborne W and/or Co. Additionally, Fallon is distinctive from the public health perspective by its cluster of childhood leukemia. The fact that these two distinctions co-occur in a small town begs the question: are childhood leukemia and exposure to airborne W and Co related causally? This question merits further investigation, namely biomedical research directly testing the effects of exposure to airborne W and Co on appropriate subject models.

Critical evaluation of research is an important element of science. As one form of critical evaluation, comment-reply about an article can serve a useful purpose by clarifying details of published research (Krausman et al., 2003). However, comment-reply does not necessarily constitute follow-up research, such as that which is called for in Fallon. Much research remains to be done in Fallon related to its cluster of childhood leukemia; it is to be hoped that it proceeds in due course.

References

ACGIH, 2001. Documentation of the Threshold Limit Values and Biological Exposure Indices, seventh ed. American Conference of Governmental Industrial Hygienists, Cincinnati, OH.

ACGIH, 2003. TLVs and BEIs based on the Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices. American Conference of Governmental Industrial Hygienists, Cincinnati OH.


