that the lipid content in breast milk and placenta was higher in Finnish than in Danish samples (Shen et al. 2007). Country of origin was therefore included as a covariate in a binary logistic regression. We found no significant difference between mothers with and without diabetes for fat content in breast milk or placenta (p = 0.975 and 0.107, respectively) or the sum of the most prevalent BDE congeners (p = 0.233 and 0.317, respectively). However, the number of diabetic mothers in our data set is too small to draw any firm conclusions from these results.

In conclusion, the association between perinatal exposure to PBDEs and congenital cryptorchidism was significant after exclusion of diabetic mothers. Exposure to environmental chemicals is, however, one of many adverse factors that alone, or in combination with each other, may cause testicular maldescent (Main et al. 2007). These additional factors include gestational complications, lifestyle, and genetic factors (Virtanen et al. 2007).

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Tungsten and Cobalt in Fallon, Nevada: Association with Childhood Leukemia

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In their article, Sheppard et al. (2007) suggested that the "results in Fallon [Nevada] suggest a temporal correspondence between the onset of excessive childhood leukemia and elevated levels of tungsten and cobalt." Although the authors reported some interesting findings from their dendrochemistry (tree ring) analysis, the results, as presented, do not support their conclusion. In fact, if the data they report demonstrate anything, it is that the levels of tungsten in the environment are not causally associated with the cases of leukemia.

Sheppard et al.'s (2007) primary premise is that levels of tungsten increased in Fallon relative to selected comparison towns beginning in the mid-1990s, which the authors contend predates the "1997 onset" of the increased incidence of acute lymphocytic leukemia (ALL) in Churchill County. In fact, when the appropriate comparison is made, the data of Sheppard et al. show that the purported increase in environmental tungsten in Fallon occurred long after the onset of these leukemia cases (i.e., after 2001). Thus, the data they gathered supports the conclusion of the Agency for Toxic Substances and Disease Registry (2003) that the evidence does not support any link between tungsten and these leukemia cases.

Unfortunately, Sheppard et al. (2007) did not provide the actual data in their article, and they did not include error bars or standard deviations for the data points. Regardless of these defects in data presentation, careful interpretation of the graphic representations of the data yields several important insights [the tungsten concentrations listed here are approximate and were obtained from interpolation of the data points from the figures of Sheppard et al. (2007)].

First, tree ring tungsten concentrations in Fallon cottonwoods ranged from 40 to 70 ppm between 1989 and 2000, and then increased to 180 ppm in the 2001–2004 time period. Sweet Home, Oregon, cottonwoods followed a similar pattern, ranging from 50 to 75 ppm between 1989 and 2000 and increasing to 110 ppm for the 2001–2004 period. Thus, no significant increase in tungsten in cottonwood tree rings was observed at either location until the 2001–2004 period, well after the "onset" of the leukemia cases; 12 of the 15 leukemia cases (80%) had been diagnosed by the end of 2000 [Centers for Disease Control and Prevention (CDC) 2003].

Second, it appears that the "comparison town" data comprise the Douglas-fir data from Crawfordsville, Oregon, and data on Douglas-firs and cottonwoods from Sweet Home. Sheppard et al. (2007) acknowledged that "temporal variability of tungsten is higher in the cottonwoods than in the Douglas-firs," and Douglas-firs exhibit "damped temporal variability." This is likely to be at least partially due to physiologic differences of tree species (Sheppard et al. 2007). Comparing tungsten levels in responsive cottonwoods in Fallon to groups of trees from comparison towns that included less responsive Douglas-firs is an "apples-to-oranges" comparison, and any differences are more likely related to the differences in tree species than to different levels of environmental tungsten. This uncertainty is further exacerbated by comparing trees from vastly different environments—the temperate, agricultural areas of northwestern Oregon and the high desert of western Nevada.

Third, Sweet Home cottonwoods exhibited an average of 62 ppm tungsten between 1989 and 2000. Fallon cottonwoods had an average of 60 ppm during this same period. The purported temporal variability between the two locations is nonexistent when like species are compared.

Finally, according to Sheppard et al. (2007), the 1989–1996 period represents two time periods that "predate the 1997 onset of excessive leukemia …." Yet, compared with those in Fallon, the Sweet Home cottonwoods exhibited slightly higher tungsten concentrations over the 1989–1996 period. Thus, according to the data of Sheppard et al. (2007), environmental tungsten was actually lower in Fallon than in Sweet Home during the period leading up to the diagnosis of the Fallon leukemia cases.

In summary, a critical evaluation of the data leads to a radically different conclusion than that presented by Sheppard et al. (2007). Assuming that the data presented in the article are correct and reflective of environmental conditions in the Fallon area, the data indicate that the purported increase in tungsten levels (if in fact any increase occurred) occurred well after the "onset of the excessive childhood leukemia" and was not unique to this town. This interpretation is consistent with, and further supports, the conclusions that tungsten was not associated with the ALL cluster reached by the CDC in their *Cross-Sectional Exposure Assessment in Fallon* (CDC 2003; Rubin et al. 2007).

The authors provide consulting services for Kennametal, Inc., a company with a tungsten-carbide production facility in Fallon, Nevada.

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Tungsten and Cobalt: Sheppard et al. Respond

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First and foremost, our data from Nevada (Sheppard et al. 2007c) should not be quantitatively compared with that from Oregon. We did not make such a comparison in our article; to reinforce separation of these two studies, we described the results in separate subsections and presented data in separate figures. Our Oregon study was an independent test of dendrochemistry for establishing temporal patterns of environmental tungsten in a town with known emission of airborne tungsten. Tungsten emission in Sweet Home, Oregon, began in November 2000, and tree-ring tungsten in cottonwoods near the emission source increased at that time relative to comparison towns in central Oregon. This test demonstrated that dendrochemistry accurately depicts tungsten availability, at least when using cottonwoods. Therefore, dendrochemistry, especially when using cottonwood trees, can be trusted to accurately depict tungsten availability in Fallon, Nevada, where timing of emission of tungsten particles is not known with certainty.

The comparison of real interest was between Fallon and other towns of west-central Nevada. Tree-ring tungsten in Fallon was not significantly different from that of other towns of west central Nevada during the tree-ring period centered on 1991 [Figure 4 in our article (Sheppard et al. 2007c)], before the onset of the leukemia cluster. During the tree-ring period centered on 1995, corresponding to just before the onset of the leukemia cluster, Fallon tree-ring tungsten began trending upward and was significantly higher than Nevada comparison towns. During the following two time periods, overlapping temporally with the childhood leukemia cluster, Fallon tree-ring tungsten continued trending upward and remained higher than Nevada comparison towns, with significance levels at or near $p = 0.05$ (we provided p-values in place of error bars), thus indicating the temporal correspondence between elevated tungsten in Fallon and the childhood leukemia cluster.

The Centers for Disease Control and Prevention (CDC) conclusion that tungsten is not mathematically associated with the leukemia cases of Fallon (CDC 2003) is based on case-comparison testing within Fallon. This does not rule out that an underlying association actually exists but is not detectable by the case-comparison technique. Granted, no relation was reported between leukemia and tungsten exposure, but exposure to tungsten was found to be community-wide, with levels being high both in case children and families and in comparison children and families (CDC 2003). In other words, there was little to no variability in exposure at the community scale (i.e., most everyone in Fallon has been exposed) but high variability in onset of disease (i.e., some people got leukemia but others have not). When variability of an exposure is low relative to individual susceptibility to a disease, genetic studies are needed to identify gene polymorphisms that might make sick children more susceptible to effects of the exposure (Steinberg et al. 2007).

Our environmental research in Fallon has followed an ecologic approach with the philosophy that greater variability in exposure between different towns is more important than the minor variability in exposure within communities (Sheppard et al. 2007a). The entire town of Fallon has been compared environmentally with other towns of west-central Nevada. Multiple environmental indicators have been used, such as outdoor airborne particulates (Sheppard et al. 2006), lichens (Sheppard et al. 2007d), surface dust (Sheppard et al. 2007b), and tree rings (Sheppard et al. 2007c). These indicators incorporate environmental conditions differently from one another, yet they have corroborated one another in showing that airborne tungsten is elevated in Fallon relative to other towns of west-central Nevada or the surrounding desert. Additionally, airborne tungsten particles in Fallon have been identified as anthropogenic in origin, and not natural (Sheppard et al. 2007e).

Even with this preponderance of evidence showing spatial and temporal patterns of airborne tungsten in Fallon, we still have not concluded in any of our reports on Fallon that exposure to tungsten causes leukemia. Quite the opposite: We have acknowledged that environmental data alone cannot lead to such a conclusion and that direct biomedical testing is needed to establish a causal linkage between tungsten and leukemia.

Years ago in an article on disease cluster research, Shimkin (1965) stated that cooperation of industrial management is needed to identify and reduce environmental carcinogens. This comment still rings true today. Kennametal Inc. (Fallon, NV) claims that it supports research in Fallon aimed at understanding the childhood leukemia cluster there (Goodale 2005), but its support is apparently selective. We hereby encourage Kennametal to engage in reasonable dialogue about research in Fallon related to the childhood leukemia cluster.

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Erratum

The April 2008 Focus article [Environ Health Perspect 116:A160–A167 (2008)] includes a misprint. The first paragraph under the subhead "How Much Is Enough?" should read: "Gilchrest points out a problem with the literature: 'Everyone recommends something different, depending on the studies with which they are most aligned. One study reports an increased risk of prostate cancer for men with 25(OH)D levels above 90 ng/mL, for example [in contrast with the idea that more vitamin D is more protective against cancer].'" *EHP* regrets the error.