Direct Measurement of Lead in Bone
A Promising Biomarker

Chronic excessive exposure to lead is widespread in industrialized societies. In the United States, an estimated 3 million young children have a blood lead level of 0.50 μg/dL (10 μg/dL) or more, the level considered by the Centers for Disease Control and Prevention to indicate increased absorption. Also, more than 1.4 million industrial workers have the potential for chronic exposure through occupations such as stained glass manufacturing, battery making, and bridge demolishing.

Despite the extent of this exposure, great gaps exist in our knowledge of the chronic toxicity of lead. For example, we do not know the level of cumulative exposure in adults that is associated with chronic dysfunction of the central or peripheral nervous systems. We do not know whether chronic exposure is associated with motor neuron disease, Parkinsonism, or other chronic neurological illnesses. We do not know the fraction of hypertension or of renal failure that may be attributable to elevated lead levels. In women, we know little about the toxic consequences of the lead mobilization that may occur during pregnancy, lactation, and menopause. In men, we do not know the level of exposure that may be associated with disordered spermatogenesis or other reproductive dysfunctions.

Lack of a sensitive and specific biologic marker of cumulative exposure has long been an impediment to research in this field. The fundamental problem is that the blood lead level, the traditional index of absorption, reflects only relatively recent exposure because the half-life of lead in blood is only about 36 days. In persons with chronic exposure, there is little correlation between a single, randomly obtained blood lead level and either a cumulative index of absorption or the body burden lead.

Now comes a technology—x-ray fluorescence (XRF) analysis of lead in bone—that appears to hold substantial promise for overcoming those limitations. The XRF technique, as reported in this issue of The Journal by Kosnett et al., takes advantage of the fact that absorbed lead is stored in bone and has a half-life in dense cortical bone of at least 25 years. Thus, it is hypothesized that direct measurement of lead in bone will provide data on past exposure and that these data will be useful in epidemiologic analysis as well as for clinical assessment. The XRF technique is noninvasive, relatively quick, and involves less than 2.5% of the radiation of a chest x-ray examination.

Two XRF technologies have been described: x-ray fluorescence (KXRF) and L x-ray fluorescence (LXRF). The KXRF technology has been more widely used and better validated. It measures lead approximately 1 mm into bone. Therefore, it provides data on the total amount of lead across the bone. The results are expressed in micrograms of lead per gram of bone mineral (or in parts per million lead in bone). This is the technology used by Kosnett et al. The LXRF technology has been validated by assessing lead concentrations in doped plaster of paris bone models and in cadaver samples. Additionally, the technology has been validated in vivo, in that a high correlation (r=0.84) has been found between the concentration of lead in bone and an index of cumulative exposure in persons who had repeated blood lead testing in the work setting? The LXRF technology, which has been used only in some pediatric studies, measures lead only 2 to 3 mm into bone. Unlike KXRF, this technique is highly sensitive to slight variation in thickness of the skin overlying the bone and is sensitive also to movement. The theoretical advantage of LXRF is that it may provide specific information on lead levels in subperiosteal bone. Lead in subperiosteal areas may be more easily mobilizable than lead in dense cortical bone and may therefore more rapidly reflect environmental and physiological changes.

Epidemiologic and clinical studies that have long been difficult will become more readily feasible with XRF technology. One application will be further validation of the heroic studies by Needleman and his colleagues on the chronic neurological toxicity of lead.11 The early reports by Needleman et al10 used tooth lead, as measured by XRF, as the indicator of chronic exposure. In this remarkably thorough series of investigations, it has been shown that lead is toxic to the nervous system of young children at very low levels. The work has been corroborated already by prospective epidemiologic studies undertaken in Cincinnati, Ohio, Australia, and Europe.14 With use of XRF, it will be possible to examine the chronic neurological toxicity, as well as in children by assessing dose—response measurements of lead in bone. The XRF technology may be useful also in assessing the contribution of lead to neurological and psychological dysfunction in adolescents who manifest symptoms of developmental delay, learning, or criminality.
The XRF technology has many potential applications for improved diagnosis and for disease prevention. For example, in working populations chronically exposed to lead, the accepted approach for lead poisoning prevention consists of serial measurement of the blood lead level with periodic temporary removal from exposure when the level exceeds the legal limit. The danger inherent in this approach is that the body burden may become substantial with continuing exposure. With XRF technology, it now will be possible to assess cumulative lead absorption in workers and determine whether it results in chronic disease. Preventive strategies may need to be reassessed. Other applications may include assessment of bone lead levels in newly diagnosed hypertensives, in women planning pregnancy, or in men experiencing reproductive dysfunction.

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