Innovations

X-ray Fluorescence Analysis of Lead in Bone

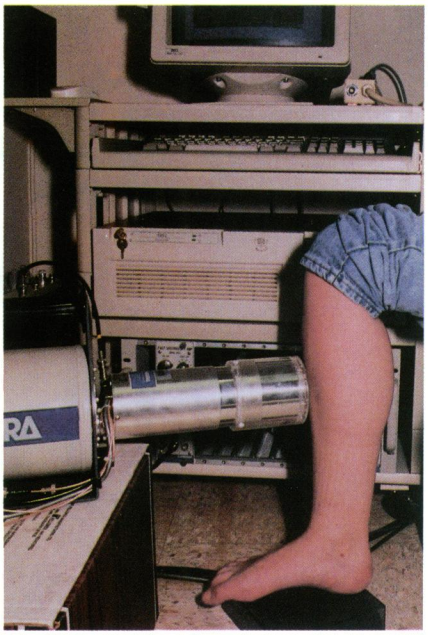
The *in vivo* measurement of lead burden in human bones by X-ray fluorescence (XRF) analysis is a newly developed, noninvasive, and relatively rapid approach to assessing chronic lead exposure. XRF takes advantage of the fact that bone is the storage tissue for lead in the human body and that lead in bone has a half-life of decades.

All measurements of lead in bone use radiation, which makes the radiation dose and its risk important considerations. The dose of radiation delivered by any measurement technique is small. Nevertheless, full radiodosimetric analysis of the cadmium-109-based K XRF and L XRF methods has been performed. The differences between the radiation doses received with the two methods are less important than their magnitude; for ^{109}Cd K XRF the effective dose for a one-year-old child is equivalent to approximately three hours of the average annual effective dose arising from background radiation. The additional risk of a cancer mortality (excluding leukemia) imposed by this measurement is approximately 1 in 10 million. Thus, radiation risk is not a limiting factor in either XRF method.

XRF analysis may be undertaken using either K or L X-rays, and both K and L XRF systems have been developed. The K method has several intrinsic advantages over the L method. First, the K-XRF method samples lead across the entire transverse section of bone, in contrast to the L method, where the sensitivity falls by 70% 1.3 mm into bone. There is evidence that lead is not homogeneously distributed in bone, if there is variation in the concentration of lead across the bone between the superficial, subperiosteal, and the deeper sectors, then the L measurement will fall victim to this variation, whereas the K will not. Additionally, the ^{109}Cd-based K method does not require measurement of the thickness of the overlying skin, whereas the L method is exquisitely sensitive to any error in measurement of skin thickness. A third methodologic advantage of the K method is that it is relatively resistant to movement of the subject during the sampling period: given that the typical sampling time is approximately 15 minutes, this consideration is not trivial. In defense of the L method, there may be detailed modeling studies in which it is desirable to simultaneously examine lead content in several bone compartments. In such circumstances, the combined use of the K and the L instruments might offer unique information on the kinetics of lead in both the superficial and deeper compartment of compact bone. However, the K-XRF instrument is the single best tool for assessing of the chronic toxic effects of lead in epidemiological studies.

Both K and L XRF methods have been validated, in both cases by comparing XRF and atomic absorption spectrometry (AAS). The K XRF was validated by indirectly comparing, for example, bare bone samples from which a core had been removed for AAS analysis before the K XRF measurement. XRF and AAS methods were independently calibrated. The L XRF technique was validated using amputated, intact human limbs, first with the overlying tissue intact, then with the tissue removed. Bone samples were then independently measured by AAS.

With the application of XRF technology to epidemiologic and clinical studies, the toxicology of chronic lead exposure in adults can be explored with a sensitivity and specificity that has not heretofore been possible. Answers will be provided to basic questions about whether there are toxic effects at low doses of lead in adults or whether there are thresholds of toxicity below which no toxic effects are detectable.

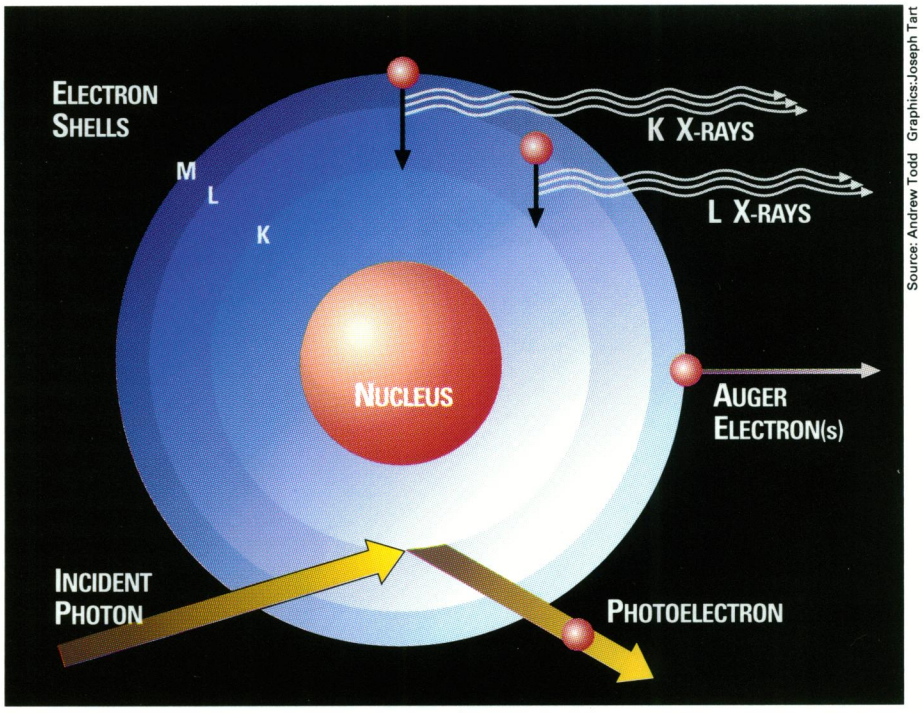


Andrew Todd

Aim and fire. New machine generates X-ray fluorescent signals in a noninvasive method for measuring lead in bones.

XRF will also enable the examination of the possible influence of genetic polymorphism on chronic lead toxicity with a sensitivity and specificity never achieved.

In longitudinal prospective studies of populations exposed to lead, XRF methods may be particularly useful. Two groups in



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Two approaches to a common problem. X-ray fluorescence technique quantifies energy generated in K and L electron shells to analyze lead in bone.

whom prospective studies may be most valuable are new employees in the lead industry and retirees or striking workers, who are no longer exposed to lead, but who had many previous years of lead exposure. In each of these groups, use of the XRF technology will permit examination of either accumulation or loss of lead over time.

The toxic endpoints that might be most fruitfully evaluated in prospective epidemiologic studies of workers include toxicity to the peripheral and central nervous system, renal toxicity, reproductive toxicity, and lead-induced hypertension. Such prospective studies would build upon and follow previous cross-sectional epidemiologic studies.

XRF bone lead measurements will be important for assessing intervention in lead poisoning. For example, in workers undergoing therapeutic chelation, XRF measurements will document successful removal of lead from bone. In such studies, the use of K and L instruments simultaneously to assess the movement of lead from various compartments in bone as the result of chelation would provide extremely important data. Additionally, it would be important in such studies to correlate the loss of lead from various bony compartments with improvements in the function of various organs, including the nervous system, the kidneys, and the reproductive organs.

Finally, XRF technology will be extremely important for refining existing models of the pharmacokinetics of lead. One of the most useful models of the body burden and pharmacokinetics of lead was developed by Bernard and refined by Hattis (see Suggested Reading). The model posits the existence of five functional compartments. However, only limited experimental validation of this model is available at present.

Suggested Reading

Bernard SR. Dosimetric data and metabolic model for lead. Health Phys 32:44–46 (1977).

Christoffersson JO, Ahlgren L, Schütz A, Skerfving S, Mattsson S. Decrease of skeletal lead levels in man after the end of occupational exposure. Arch Environ Health 41:312–318 (1986).

Hattis D. Dynamics of medical removal protection for lead—a reappraisal. Technical report CPA-81-245. Cambridge, MA:Massachusetts Institute of Technology, 1981.

Landrigan PJ. Current issues in the epidemiology and toxicology of occupational exposure to lead. Environ Health Perspect 89:61–66 (1990).

Landrigan PJ. Strategies for epidemiological studies of lead in bone in occupationally exposed populations. Environ Health Perspect 91:81–86 (1991).

Todd AC, McNeill FE, Fowler BA. In vivo X-ray fluorescence of lead in bone. Environ Res 59(2):326–335 (1992).

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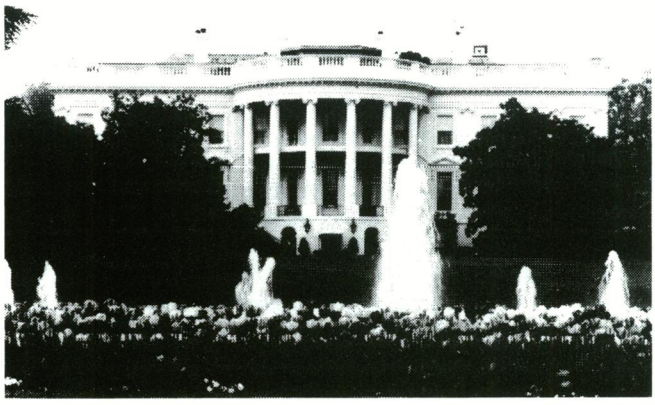

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