Lead Testing and the Public Health Lead Screening Program

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Lead Exposure

Lead is a naturally occurring element that has found use in metal materials throughout history. The atomic symbol for lead, Pb, is derived from the Latin word *plumbum*, for the weight used in a surveyor's plumb line. Lead can be found in concentrated ore deposits in the earth, and its compounds are thus often a detectable component of the natural environment in most regions of the world. As such, there is low-level exposure of humans to lead, as evidenced by the fact that lead can also be detected in blood and tissue in virtually everyone. There it may be regarded as a contaminant, in the sense that lead has no known physiologic or metabolic role. Unfortunately, lead is not chemically inert, and its reactions with organic molecules, both specific and nonspecific, can lead to toxic effects at high and even relatively low levels of exposure.

Toxic Effects of Lead

Specific effects of lead include inhibition of enzymes in the heme synthesis pathways used to produce functional hemoglobin, the oxygen-carrying molecule that is packaged in red blood cells. Thus, one hallmark effect of chronic toxic lead exposure is anemia. Nonspecific toxic effects of lead are also deleterious to health. Like other metals, lead can bind nonspecifically to proteins. It is for this reason that excess lead exposure can cause buildup of lead in tissues. Lead binding to protein can disrupt intramolecular bonds that are necessary for the proper structure and function of the protein. And, because circulating lead is excreted through the kidney, kidney function is particularly susceptible to the toxic effects of this metal, in either chronic or acute overexposure. The nervous system is also susceptible to deleterious, nonspecific effects of lead that can cause a decrease in nerve conduction velocity. Importantly, chronic exposure even to relatively low levels of lead can have negative effects on various aspects of development in children (such as hearing and growth). Acute, high-level exposure to lead can cause encephalopathy and death.

Acute toxicity due to lead exposure requires treatment. In addition to medical management of kidney failure, treatment consists of chelation therapy. Chelation is the removal of metal ions by a medication that has a high affinity for the metal. A number of chelating agents are available to treat lead toxicity. Chelation therapy can rapidly remove lead from the blood, and thereby prevent any further deposition into tissues. However, the therapy has less effect on the rate of removal of lead from tissues. This is evidenced by the "rebound" of circulating blood levels to higher values after cessation of chelation therapy. Nonetheless, chelation therapy is an important component of management in cases of acute toxicity. Chelation therapy is recommended for circulating blood levels of > 45 μg/dL (2.2 μM). Therapy is monitored by documenting increased rates of lead excretion in urine.

Public Health Lead Screening Programs

The goals of public health lead screening programs are to identify individuals who have a higher than expected blood lead level, and to find and remove sources of exposure. Exposure is primarily due to the former use of lead in household paints. In recognition of this issue, and based in part on evidence of undue exposure among children, the Centers for Disease Control (CDC) in 1997 issued specific guidelines for public health lead screening programs (see Web References 1). This document, and ongoing summaries of the statistics and demographics of lead screening given periodically in the CDC's *Morbidity and Mortality Weekly Report*, provide detailed history of the public health concern and intervention in lead exposure. The guidelines

define elevated blood lead concentration as > 10 µg/dL (480 nM), and recommend that screening by public health programs be targeted to those children most vulnerable to undue exposure. A CDC publication specifically addresses targeting of Medicaid patients as a high-risk group (see Web References 2).

Measurement of Lead in Whole Blood

Because lead in blood is concentrated in erythrocytes, screening tests are conducted using whole blood rather than serum or plasma. Blood lead is conventionally analyzed by one of two methods, either atomic absorption (AA) or anodic stripping voltametry (ASV). AA is analogous to simple absorbance spectrophotometry. The sample is volatilized by a furnace apparatus. Absorption of light of a specific wavelength characteristic of lead is measured and compared to a standard curve from which the sample lead concentration is determined. ASV is based on electrochemistry. As current is passed through a circuit that includes the liquid sample, the instrument's anode tip becomes plated by metals from the sample. Reversing the process strips the anode of specific metals at specific voltages, and the current generated at the characteristic voltage for lead enables determination of the original lead concentration by comparison to a standard curve. AA has the advantages that it can be automated and requires only infrequent calibration if properly maintained. The capital investment and maintenance required for AA is significantly greater than that for ASV, however.

Analytical proficiency surveys provide a national peer review measure of quality control for lead testing. They also provide excellent data for comparison of AA and ASV methods. Both AA and ASV yield accurate and reliable measurements of lead concentrations, as evidenced by data from the College of American Pathologists (CAP) surveys and by the Wisconsin surveys (a program that is administered by the U.S. Public Health Service). As shown in **Figure 1,** lead concentrations determined by AA and ASV are statistically indistinguishable. Data from NPHL are indistinguishable from national data (**Figure 2**). The "coefficient of variation" (CV), a measure of analytical precision, is between 5% and 10% for both ASV and AA at all but low lead concentrations.

An individual proficiency survey result (a singleton measurement of a sample) will meet CDC acceptability criteria if its value is *(a)* $\pm$ 10% of the mean, or *(b)* within $\pm$ 4 µg/dL from the mean, whichever range is greater. For example, given a mean value of [Pb] = 10 µg/dL (the cutoff value for a positive screening test, and for which the CV is approximately 10%), 95% of the survey results will typically be between 8 and 12 µg/dL - a difference of 50% between low and high values, but well within the acceptable range of 10 $\pm$ 4 µg/dL It is important to note that such differences are unlikely to have any distinct medical significance. Such uncertainty is an inherent aspect of any analytical procedure, and it is a known component of screening procedures that use singleton measurements with a fixed (and usually conservative) cutoff value for positive results.

Results from the Lead Screening: Program in Douglas County

Public health-sponsored lead screening has been conducted by Douglas County for more than three years. Data provided by Douglas County for the fraction of positive screens ([Pb] > 10 µg/dL) from among all screening tests is shown in **Figure 3**. Two aspects of these data are striking. First, there is a yearly cycle in the number of positives, with higher positive rates in late summer and lower positive rates in late winter. This presumably reflects increased exposure of children to lead during the outdoor summer months. Second, the data clearly demonstrate a continuous decrease in the screening test positive rate since the inception of the program. A national trend of decreasing positive rates in lead screening tests has been noted by the CDC (Update: Blood Lead Levels --United States, 1991-1994. *MMWR* 1997; 46(7):141-6) and was attributed in part to programmatic success in the removal of lead from common environmental sources of exposure. Additionally, the trend in Douglas County may in part reflect an expansion of the program to include a greater fraction of low prevalence populations. The absolute numbers

of screenings has increased over this period from approximately 200/month to approximately 500/month, and the demographic characteristics of the expanded population are likely also to have broadened during this time.

Importance of Proper Specimen Collection

Proper specimen collection is an essential component of the success of the lead screening program. We all recognize that collection of blood from children can be a difficult task! Nonetheless, only a small volume is required (200 µL). It is important that the sample be properly anticoagulated after collection by mixing of the contents of the collection with the anticoagulant in the collection tube. Instructions for proper collection techniques are available from NPHL. A detailed discussion regarding collection procedures is also available in the CDC lead screening program guidelines. As with all patient specimens, it is good practice to send the specimen to the laboratory for testing without delay.

The Future of Lead Screening

A successful screening program will eventually result in eliminating sources of childhood lead exposure, whether in the home or playground. Development of a portable blood lead analyzer for use outside of the laboratory could greatly assist screening efforts. Interventions to reduce lead hazards include improving the quality of housing (e.g., improving standards for rental property, maintenance and cleaning), and programs for better education and awareness about lead. Citizens and public health agencies must work together toward these goals in order to build upon the successes achieved to date.

Web References

1. http://www.cdc.gov/nceh/lead/guide/guide97.htm
2. http//www.cdc/mmwr/PDF/RR/RR4914.pdf

Figures 1, 2 and 3:

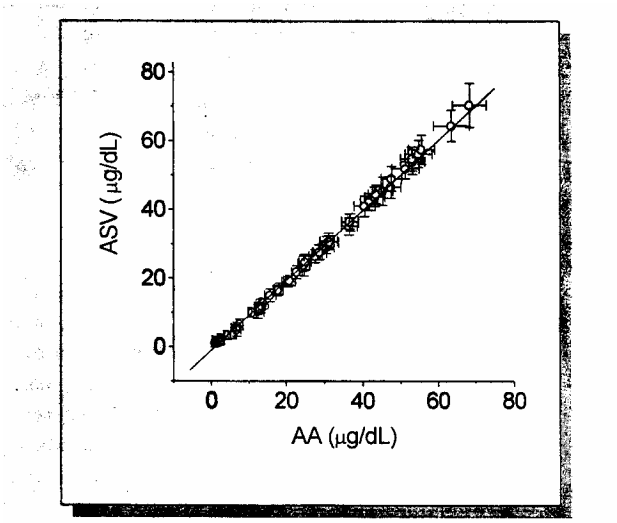

Figure 1. Comparison of national survey results for ASV and AA measurements of blood lead.

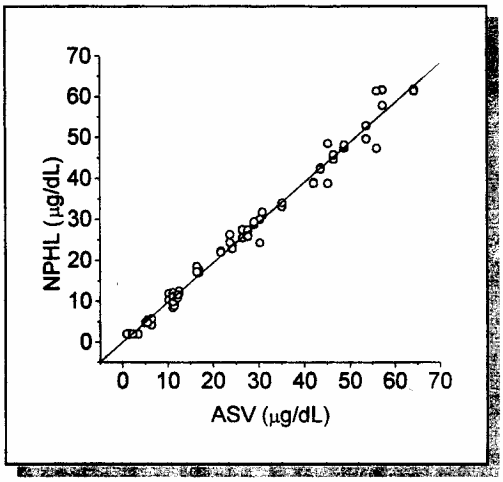

Figure 2. Comparison of NPHL survey results using ASV and national survey results using ASV.

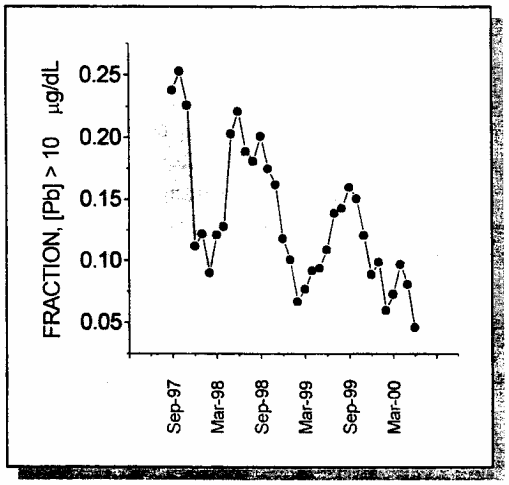

Figure 3. Cycle of positive lead screens.