Filter Paper Lead Testing

Lead is a common toxic metal in our environment. It is present at high concentrations (up to 600 g/kg) in some paints manufactured before 1970. Some artistic ceramic products and leaded glass contain substantial amounts of lead that can be leached by weak acids such as vinegar and fruit juices. Lead is also found in dirt from areas adjacent to buildings painted with lead-based paints and on highways, where it has accumulated from previous use of leaded gasoline in automobiles. Water transported through lead or lead-soldered pipe contains some lead, with higher concentrations found in water that is acidic. Some traditional home medicines contain lead. As a result of all of these opportunities for exposure, a person may be exposed to lead ranging from 5 to 200 μg per day in the United States, of which 1–10% is absorbed. Children may absorb as much as 50% of the dietary intake, and the fraction of lead absorbed is enhanced by nutritional deficiency. Exposure to lead from any of these sources by ingestion, inhalation, or dermal contact can contribute to significant toxicity.

The finding that lead body burden contributes significantly to decreased intellectual capability in children is of considerable interest and concern (1). Young children have greater opportunity for exposure because they tend to spend time on the floor of the building they are in; in older homes previously treated with lead-based paints, lead-laden paint chips and dust accumulate on the floor where children are likely to pick them up and put them in their mouths.

Guidelines published in the United States by the Center for Disease Control and Prevention (CDC) indicate that measurement of lead in whole blood is the preferred test for detecting lead effects in children (2). Chronic whole blood lead concentrations <0.49 μmol/L (10 μg/dL) are considered acceptable in children. The CDC recommends that chelation therapy be considered when the whole blood lead concentration exceeds 1 μmol/L (20 μg/dL) in children, and chelation therapy is indicated when whole blood lead is ≥2.25 μmol/L (45 μg/dL). The World Health Organization has defined whole blood lead concentrations >1.5 μmol/L (30 μg/dL) in adults as indicative of significant exposure and recommends chelation therapy when the whole blood lead concentration exceeds 3 μmol/L (60 μg/dL). As a result of these national and international guidelines, blood lead analysis has become the norm for identifying individuals with excessive body burden of lead.

Blood collected by venipuncture limits the opportunity for specimen contamination to the small exposure that occurs as the venipuncture needle punctures the skin surface. Collection of blood into a vacuum blood collection container also serves to sequester blood from environmental contamination (3). Capillary blood collection can be substituted for venous sampling, but rigorous wound site cleansing is necessary to preclude blood contamination (2–5). Even with stringent finger cleaning and the use of barrier sprays, a potential for blood contamination exists (4, 5). In general, higher concentrations have been reported for capillary samples than for venous (4–6), leading to increased false-positive rates. The observed difference between venous and capillary lead concentrations is thought to be attributable to specimen contamination from lead present on the skin surface.

Because venipuncture is threatening to children and because whole blood is somewhat unstable, alternative means of specimen collection, stabilization, and transport have been evaluated. In 1970, Delves (7) introduced a microsampling technique for measurement of lead in biological samples with use of a platinum crucible; the “Delves cup” technique was one of the first to provide accurate assessment of low lead concentrations in complex biological matrices. The application of this technique to the screening of blood samples for lead concentration using filter paper punched discs was reported by Cernik (8).

As a result of these works, the method of collecting blood spots dried on filter paper (FP) for lead analysis became attractive for mass screening of children to assess lead exposure. FP blood lead (FP-Pb) analysis is of interest because of the following potential advantages: (a) a relatively small amount of blood is required; (b) blood collection via finger stick is generally easier and less traumatic to children; (c) collection can be performed by a relatively untrained collector; and (d) appropriately prepared FP specimens are stable and can be easily transported to the laboratory (9, 10).

Substitution of FP collection of capillary blood introduces considerable opportunity for preanalytical variables. In addition to the surface contamination mentioned above, low extraction recoveries of lead from FP have been reported (6, 9, 10), and nonreproducibility of blood spotting because of differences in hematocrit and hemoglobin has been noted (8, 11, 12). Bias may be introduced by high and variable lead content of the FP or by contamination encountered in the sampling process itself because blood must be dropped onto the FP and air dried (6, 9, 13, 14).

We believe that the technique of spotting blood on FP and subsequent extraction can be made to work under controlled laboratory conditions. This has been confirmed by individuals working in the field many years [Delves, personal communication, and Refs. (5, 6)]. But collection of whole blood on FP in the field adds a significant variable of contamination to the process.

In this issue, Stanton et al. (15) describe their experience with a Pilot Proficiency Testing Program for laboratories supporting FP-Pb testing. Stanton and colleagues are well-known for their work with blood lead proficiency testing, having many years of experience providing recognized proficiency testing programs offered by the Wisconsin State Laboratory of Hygiene. In this issue, Stanton et al. (15) conclude that “properly utilized FP testing methods can accurately measure blood lead concentra-
tion”. We do not believe that this conclusion can be extrapolated to routine practice because it is based on a fundamental limitation in the program—the sponsors prepared the samples on the same paper source for all laboratories in a rigorously controlled environment. This approach tests only the laboratories’ ability to extract and measure lead from paper but does not test the laboratories’ ability to collect a clinically valid sample in a routine collection environment. The Pilot Proficiency Program reported by Stanton et al. (15) is limited because it does not address the significant preanalytical variables described in previous paragraphs.

We note that the early phase (October–December 1997) of the study by Stanton et al. (15) was performed on FP provided by participating laboratories, whereas the later part of the study (January–July 1998) was performed using a single FP source (Schleicher & Schuell filter paper no. 903). We observed the significant variability evident in Fig. 1 during the months of October and November 1997, when laboratories provided their own testing paper, and compared it to the lesser variability observed after December 1997, when the proficiency testing center spotted blood on one source of FP. A radical improvement in imprecision was observed after December 1997; that interval reflects the time when the FP substrate was changed.

The authors suggest that the decrease in imprecision was attributable to improvements implemented by laboratories after seeing their preliminary field-test data. It seems more likely that the improvement noted reflects the singular source of paper that was used after December 1997. The imprecision noted in Fig. 1 during the early phase includes the FP variable, whereas the data after December 1997 remove the FP variable. Significant imprecision was observed before, but not after, this FP variable was removed. We suggest that the various sources of FP are likely contributors to the significant imprecision noted in the early phase of the study. The early phase of the study more closely reflects the realities of routine specimen collection, whereas the later phase of the study represents an artificial environment that is not achieved in day-to-day practice.

We believe that FP, spotting technique, and surface contamination of capillary blood are sources of significant variability in FP-Pb testing. Others have reported similar experiences [Delves, personal communication, and Refs. (3, 5, 6, 11, 14)]. The Stanton Pilot Proficiency Testing Program is limited because it does not consider the preanalytical variables in reaching its conclusion that FP-Pb testing can accurately measure blood lead concentration. It is our opinion that the study shows only that laboratories can extract and measure lead from uniformly prepared FP with reasonable imprecision. Readers should not conclude that the report of the Stanton Pilot Proficiency Program represents an endorsement that FP-Pb testing is a suitable replacement for venous blood lead testing. FP-Pb testing is a variable technology that demonstrates significant imprecision when used in clinical practice. Clinical laboratorians should continue to approach this technology with caution.

References

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