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ABSTRACT

In response to the increased demand for reliable alternatives to venous lead testing, the Centers for Disease Control has called for increased research into using capillary methodologies. In the past, there have been problems with this procedure, primarily because of external lead contamination falsely elevating values.

A three tiered approach was developed to assess the adequacy of capillary lead specimens. The first approach involved examination of a large database of capillary and venous samples for obvious differences. The second approach involved analysis of elevated lead followups for indications of gross contamination. The last approach involved experimentation to determine if handwashing eliminates gross contamination.

Obvious differences were found between the venous and capillary databases. Gross contamination was rare, but the data suggest variable minor contamination. The analysis of elevated lead followups demonstrated that gross contamination is sometimes present, but more likely the decrease in followup results is due to day to day fluctuations in lead levels and decreases in minor contamination. Experimentation demonstrated that handwashing greatly reduces the amount of external lead contamination.

Capillary lead testing should be considered a viable alternative to venous testing, provided that the patient and collector are meticulous in detail.

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THE ADEQUACY OF CAPILLARY LEAD SPECIMENS

by

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A thesis submitted to the faculty of
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in

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ABSTRACT

In response to the increased demand for reliable alternatives to venous lead testing, the Centers for Disease Control has called for increased research into using capillary methodologies. In the past, there have been problems with this procedure, primarily because of external lead contamination falsely elevating values.

A three tiered approach was developed to assess the adequacy of capillary lead specimens. The first approach involved examination of a large database of capillary and venous samples for obvious differences. The second approach involved analysis of elevated lead followups for indications of gross contamination. The last approach involved experimentation to determine if handwashing eliminates gross contamination.

Obvious differences were found between the venous and capillary databases. Gross contamination was rare, but the data suggest variable minor contamination. The analysis of elevated lead followups demonstrated that gross contamination is sometimes present, but more likely the decrease in followup results is due to day to day fluctuations in lead levels and decreases in minor contamination. Experimentation demonstrated that handwashing greatly reduces the amount of external lead contamination.

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INTRODUCTION

General Characteristics

Lead is a naturally occurring bluish gray soft metal. It has no characteristic taste or smell.[1] It has two valances, +2 and +4, and there are four stable isotopes of lead (mass numbers of 204, 206, 207, and 208).[2] Lead has no physiologic value.[2]

History

Lead has been an important part of the history of civilized man. Although possibly used earlier, lead has been traced back over 8,000 years in Turkey.[2] Lead was also used as a sweetener and in water pipes in ancient Rome and some have since implicated it in the decline and fall of the Roman Empire.[2,4,5] Lead was identified as a toxin by Hippocrates and Greek physicians(400 BC).[2,5] Although identified as a toxin, lead has been used in a number of medicines over the past 3,000 years, both internally and externally.[2] By the late 19th century, lead was recognized as a toxin to children in Australia.[5] Lead in paint was banned in Queensland Australia early in the 20th century when it was identified as a social problem.[5]

Lead awareness in the United States began in the early part of this century, but efforts to reduce the amount of lead in paint were not successful until mid-century.[5] Lead was introduced as a gasoline additive in the 1920s. During this time, the lead industry dominated research. It was concluded that lead occurred naturally in humans and the body did not store lead over and above what was considered natural.[5] Therefore, no relationship could occur between lead in various body compartments and lead poisoning. If lead poisoning did occur, and the patient recovered, there was thought to be no long

term effects.[5,6] In 1943, Randolph Byers argued that lead interfered with normal central nervous system development.[7] The bodies of evidence supporting lead as an important social issue began to mount.

By the early 1950s, Baltimore enacted laws concerning lead in city housing. However, these laws were poorly enforced.[5] Most of the country was slow to recognize the dangers of lead, relegating it to an acute disease of inner city children.[5] Until the mid-1960s, the levels thought to be dangerous were well above 50 μg/dL, far different from the safe levels of today (<10 μg/dL).[3] As the late 1960s emerged, and many in our nation longed for symbolic evils to latch onto, lead became the perfect vehicle.[5] Not only was it damaging to inner-city children who were already challenged by numerous circumstances, but it was also perceived that the government was doing little to alleviate this problem.[65]

Over the past 25 years, various laws and acts have been passed to reduce the amount of lead in paint, gasoline, water, and food.[1,3,5] The goal has been to reduce lead exposure, especially for children.

Sources of Lead

All who live in an industrialized environment are exposed to lead at some level. The clinical importance of this exposure varies and is dependent upon a number of factors. As a general rule, exposure occurs by four major pathways: ambient air, food, water, and dust.[97] These four will be discussed, along with minor contributors to lead exposure.

The lead in these four major pathways is derived from two main sources, gasoline and paint. Tetra-ethyl lead was introduced as an additive to gasoline in the 1920s.[5] In the past, lead emitted by automobiles was a major contributor to the concentration found in air and dust and food to a minor extent.[1] However, 99.8% lead has been eliminated from gasoline today.[8] It should be noted that this reduction has not occurred in all parts of the world and leaded gasoline is still used in farm equipment in this country.[9] Paint,

which also has been reduced in lead concentration in recent years, still is a major concern. In the first half of this century, paint was comprised of 50% percent lead and 50% linseed oil.[6] This concentration of lead in paint was somewhat reduced when the dangers of lead became known. In 1971, the legal limit of lead in paint was reduced to 1 percent and in 1977, the Consumer Product Safety Commission banned the manufacture of lead based paint containing more than 0.06% lead by weight.[3] No limitations were placed on lead paint for marine, industrial, or military use.[3] Currently, leaded paint remains the primary source of lead poisoning in young children.[6] There are currently around four million homes that have leaded paint with young children residing in them.[8] A single chip of paint can have as much as 5,000 $\mu g/cm,^2$ thus providing greater short term exposure than any other single source.[8] The ingestion of single paint chips, pica plays a much lesser role in lead poisoning than previously thought.[1]

Currently, the largest concern of lead exposure is in soil and dusts. It is estimated that over four million metric tons of lead from gasoline still remain in dust and soil, despite the drastic reduction in lead in gasoline.[3] Most of this lead is in the upper 2 to 5 centimeters of undisturbed soil.[1,3] Next to roadways, the concentration of lead in soil can reach one percent.[1] Normal soil contains less than 0.005% lead.[6] Soils in urban gardens have been shown to have elevated amounts of lead.. Concentrations of soil over 1 percent have been found adjacent to houses with exterior lead based paint.[3] Children ages one to six consume an average of 0.2 grams of lead per day in normal hand to mouth activity.[1] Some studies also suggest a significant relationship between levels of environmental lead within the home and the total lead burden of children.[10]

Another pathway of lead is the consumption of food. The amount of lead eaten by an average person has decreased dramatically in the last 15 years.[4] This decrease can be traced to the elimination of lead soldered food cans and the reduction in leaded gasoline.[8] In 1980, 47% of food and soft drink cans were lead soldered.[8] By 1991, these cans were no longer manufactured in this manner. This is important, as illustrated

by the following example. In 1986, the percentage of cans with lead solder had been reduced to around 15%, but 42% of the lead in our diet came from these cans. The elimination of this last 15% of lead soldered cans reduced the amount of lead in our diet by almost half.[8]

The average daily intake for an average two year old has declined from 30 μg per day in 1982 to 5 μg per day in 1988.[3] Some of this decrease can also be attributed to unleaded gasoline.[3] Some imported food is still sold in lead soldered cans and lead can still be found in a variety of foods the average American consumes.[3] In urban gardens, foods exposed to air while growing have approximately four times the lead concentration of those foods which grow covered.[9]

The environmental protection agency (EPA) has set a goal of less than 20 μg/L lead in drinking water.[6] Sixteen percent of households in the United States (42 million individuals) are at risk.[6,9] The amount of lead in drinking water is generally low.[1] The majority of lead in drinking water is derived from the water distribution system, where lead can leech out of lead connectors, service lines and pipes, lead soldered joints, etc...[3] In 1986, the Safe Drinking Water Act banned the use of lead in public drinking water distribution systems.[3] It is thought that lead in drinking water is absorbed more readily than lead in food (especially in adults).[1]

Since the reduction of lead in gasoline, the airborne pathway has become less important. Until recently, automobile emissions were the largest source of lead emitted in the atmosphere.[1] However, industrial processes are the current major contributor.[1] There has been a 30-fold reduction in the amount of airborne lead since the late 1960s.[11] Except around areas such as smelters and battery manufacturing plants, inhalation of airborne lead is a minor exposure pathway.[3] The human body does not retain much of the lead that is inhaled.[1] The main concern with airborne lead is the fallout that can occur. In the atmosphere, lead exists in particulate form, with varying sizes of particles.[1] They are removed from the atmosphere by wet or dry deposition. Larger particles, such

as those emitted by automobiles, settle out of the air rapidly and are deposited near the point of origin.[1] This is demonstrated by the elevated concentration of lead in soil within 25 meters of roadways.[1] Smaller particles can travel hundreds of miles.[1] Lead in the air can range from almost non existent in remote areas (7.6×10^{-5} ug/m^3 in Antarctica) to high concentrations in urban areas (> 10 ug/m^3).[7] The EPA has recommended a National Ambient Air Quality Standard of 1.5 ug/m^3. In 1988, the average lead concentration of all 139 urban monitoring sites was 0.085 ug/m^3, with all sites below recommended levels.[1]

In addition to the major sources, minor sources of lead may be obtained through bread wrappers, breast milk, cosmetics, glass, and plastics, ink from comics, boiled water used in reconstitution of infant formulas, cigarettes, certain folk medicines, and from jobs and hobbies.[1,4,9,13,14]

Uses of Lead

Lead is obtained by two methods, mining and recycling. Most mined lead comes from underground methods.[1] Lead can be sentered, smelted, drossed, and refined to a 99.95 to 99.99% purity.[1] Over 400,000 metric tons of lead was mined in 1990.[1] Recycled lead comes from a number of sources, including scrap, product wastes, refinery drosses, and residues.[1] Lead is of commercial importance due to its chemical stability in air, water, and soil, acid resistance, ease of fabrication, low melting point, high density, and its ease of casting.[1] Seventy percent of lead is consumed in the transportation industry, the majority in battery production.[1] Construction, electrical uses, ammunition, television glass and paint are the other major uses.[1,3] Despite the recent reduction of lead in gasoline, paint, and food containers, several new uses have been developed in computers and lasers.[1] Seventy to 75% of the lead consumed in the United States is considered suitable for recycling.[1] Lead that is not recycled is disposed of in landfills.[1]

Absorption and Metabolism of Lead

After exposure to lead, humans must absorb it to exhibit any ill-effects. The majority of this absorption occurrs in the gastrointestinal and respiratory tracts.[1,15] There is limited evidence to suggest that some lead is absorbed dermally.[1] In adults, most studies indicate only a small fraction, 6 to 15%, of lead is absorbed, if adequate food intake.[1] Adults absorb up to 50% of lead when only water is taken.[3] Children, however, absorb up to 50% of lead, regardless of the source.[1,3]

Several nutritional factors have been shown to influence lead absorption and toxicity. Among those commonly cited are total food intake, excess dietary fat, vitamins, zinc, iron, phosphorus, calcium, and cadnium.[1,6,16,20] Calcium and iron appear to play a significant role in lead absorption. Nutritional surveys indicate that children from lower socioeconomic groups consume less than the daily recommended daily allowance of both calcium and iron.[1] In children with lead levels greater than 60 μg/dL, the daily intake of calcium was significantly low.[1] An inverse relationship between calcium intake and lead levels has also been demonstrated at lower levels.[1] Evidence suggests that less lead is absorbed when the calcium content in food is high and less lead toxicity is incured.[16,17,18] Iron seems to compete with lead for absorption sites, limiting the amount of lead that can be absorbed.[1] Inadequate levels of iron in association with increased body burdens exacerbate the biochemical changes of lead poisoning.[1] However, some investigators have not found these relationships between iron and lead.[16]

The distribution of lead in the body has often been described as a three compartment model (blood, soft tissues, and bone/teeth).[1,17] Dietary lead that is not absorbed by the gastrointestinal tract is eliminated in feces.[1] The bloodstream receives lead from the respiratory and gastrointestinal tracts.[20] Eventually, most lead in the bloodstream is excreted in urine.[20] The half life of blood lead is 30 to 40 days.[1,15] Roughly 25% of blood lead is transferred to soft tissues, where the half life is 40 days.[1,15] A small

portion of blood lead is deposited in bone in place of calcium.[1,15] However, the half life of bone lead is considerably longer, 15 to 27 years.[1,15] Because of this long half-life, 94% of the total lead body burden in an adult is found in bone (73% in children).[1] Bone lead does not appear to be harmful while it is trapped in bone, but a labile compartment exists that allows for maintenance of an equilibrium of lead between bone, soft-tissue, and bone.[1,15] Vitamin D promotes the deposition of lead in bone, if adequate intake of phosphate.[20] Parathyroid hormone increases levels by increasing lead from the labile compartment.[62,97] Any state that mobilizes calcium from bones will also release lead.[1,15,20] An example of this mobilization is osteoporosis.[1]

Effects of Lead

The health consequences of lead in adults is well documented and extend to virtually every body system.[1] However, these aspects will not be discussed. The focus of this section will be the clinical implications that lead has upon children.

Children are at a greater risk to lead poisoning than adults due to increased absorption, a decreased immunity, and a developing nervous system.[1] Lead is measured in the fetal brain as early as 13 weeks.[21] No placental-fetal barrier has been found.[9,21] The mechanism for lead transport to the fetus is unknown.[21] Lead has been implicated in a variety of diseases and conditions including sudden infant death syndrome,[1] encephleopathy,[1,3] hepatic diseases,[1,3] impaired auditory function,[1,3] decreased growth,[1] decreased immune function,[1] congenital anomilies,[22] reduction in gestational age,[1,3] decreased birth weight,[3] decreased cognitive function,[6,23,24,25] decreased peripheral nerve fucntion[1,21,26,27,28,29] and unacceptable behavior.[1,29]. Many of the relationships between lead and these diseases are currently disputed.

The developing nervous system of a child is more sensitive to the effects of lead than adults, as evidenced by the lower threshold for encephalopathy.[1,29] However, due to the decrease of lead in our environment, encephalopathy and death due to lead is now

very rare.[3] The current debate is over lower lead levels. A number of studies have proposed that lead exposure is inversely related to IQ.[1,3,6,22,25,29] The leading proponent of this argument is Dr. Herbert Needleman. Most of these studies depict a drop in IQ of 2 to 6 points at levels of 10 µg/dL or lower. Many do not agree with these findings.[1,28,,30,31,32,33,34,35,36] They counter with their own studies showing little or no relationship between lead and intelligence, accusations of poor research design and fraud, and claims that important confounders were left out of studies. Lead poisoning, as a whole, has even been labeled an epidemic by edict.[34] Many more, while acknowledging the possible role lead plays in our society, down play it as a lesser problem. They espouse that problems such as anemia, violence, poverty, and poor nutrition are much more important.[30,33]

Lead Levels in the United States

Over the past 30 years, there has been a decrease in the concentration of lead found in the blood of average Americans. This decrease has been observed for the total population, adult and children, and within such subgroups as race, sex, urban and income status.[8] There has also been a dramatic decline in frank lead poisoning. However, due to a decreasing threshold of what is considered to be elevated, the prevalence of lead poisoning has not decreased as fast.[37] The majority of this decrease is due to the reduction of lead in gasoline.[1,3,8,11] Many studies have been performed that demonstrate thisdecrease in lead. These studies are summarized in Appendix A. With no exception, these studies show the percentage of children with lead levels greater than 10 µg/dL have greatly decreased. One study of Air Force dependents show less than one percent have a lead value greater than 10 ug/dL.[38] These studies contrast the studies of 20 years ago, where almost 90% of children had values over 10 ug/dL.[8]

One of the more interesting aspects of lead levels is the effect that seasonality plays. It has been noted as far back as 1923 that lead values and poisoning are higher in warmer

months.[22,39,40] For example, a Minnesota study found that lead was 40% higher in summer (mean of 3.5 μg/dL) than in winter (mean of 2.5 μg/dL). This difference could have implications when screening children for lead poisoning. Although this seasonality is not widely mentioned in the literature, some have come forward with possible explanations. These include an increased use of gasoline in warmer months, an increased exposure to outdoor lead sources, the influence of rain on dust dispersion, an increase in lead paint dust due to exposure from exposed window wells, the fever and acidosis associated with summer heat, and changes in lead absorption and recirculation due to the metabolic influence of sunlight on Vitamin D.[11,40] Because lead ingestion in children is a year round occurrence and the same seasonal variation is seen in adults, it is unlikely that an explanation that applies only to children is plausible. The most probable explanation is solar radiation.[40] This theory is supported by the fact that less variation in seasonal lead is seen near the equator, where less variation is seen in solar radiation. Greater variations are seen in higher latitude areas.[40] Regardless of the mechanisms, it is very important to note this seasonality.

Prevention of Lead Exposure

The ultimate goal of lead research is to prevent lead poisoning from occurring. Some argue that prevention efforts of the last 20 years have been so effective that little more needs to be done.[34] This is supported by the decrease in blood lead levels. Others believe that lead exposure should be prevented at any level.[6] Prevention can be divided into three main categories;. screening (blood lead determination, questionnaires), parental education, and the elimination or reduction of lead from the immediate environment.

The first portion of screening is the use of questionnaires, such as that recommended by the Centers for Disease Control (CDC), to identify potential lead poisoning.[3] Numerous studies have been conducted regarding the efficacy of the CDC questionnaire.

Some have found it to be effective,[41] some not effective,[9] and some have found only certain questions effective.[43]

Blood lead screening is another controversial concept that the CDC recommends. Many screening programs have been implemented. Some have had outstanding success. In California, before universal screening of low income children was implemented, only 100 children with levels greater than 25 µg/dL were identified annually. After universal screening, this number increased to over 700.[6] However, many are quick to point out disadvantages to screening. The disadvantages include the cost of testing and abatement, the few number of true positives identified, and the continuing disputes over what constitutes an elevated level.[44,45,46] One study found the cost of identifying a level greater than 10 µg/dL at $1245 per case.[14]

Parental education is another important practice. It is recommended that parents be taught such measures as dangers of remodeling, proper handwashing, flushing cold tap water before consuming, etc.[6] On study found a significant decrease in lead levels after an education program, but did not control for seasonal variation.[47] Although nutrition alone is not a preventative measure, it can help reduce the amount of lead absorbed by the gastrointestinal tract.[19]

There has become a large industry to deal with the abatement of lead. There are articles that both strongly support and strongly oppose lead abatement as a means of prevention of initial and repeat exposure.[1] One study concluded that although abatement may play a small role in the reduction of blood lead, the simple control of household dust is the much greater factor.[48] Other studies suggest that lead can actually rise after abatement.[49] Despite the conflicting evidence surrounding abatement, it still continues to be extensively used at great cost.

The CDC has recommended that prevention be accomplished by a joint effort of public and private organizations.[3] This should be accomplished by federal agencies,

state and local public health offices, health care providers, and public and private housing areas.[3]

Testing for Lead

Because the symptoms of lead poisoning are not specific, the laboratory plays a very important role in the diagnosis. Lead screening should be included in the differential diagnosis of anemia, hearing loss, behavior disorders, hyperactivity, developmental delays, and growth failure.[3] Several biomarkers have been suggested for use, but are either not specific or practical enough. These include iron status, vitamin D concentration, coproporphyrin in urine, aminolevulinic acid in serum and urine, and radiologic exams of the abdomen and tiba.[1,3,6,20] Lead from body sources such as hair, fingernails and urine have been shown to contain large amounts of contamination.[1,3,15] Lead in teeth could also be useful, but most feel that specimen collection far too difficult for a screening test.[1]

Until 1991, when the danger level was considered to be 25 µg/dL, measurement of free erythrocyte protoporphyrin (FEP) or zinc protoporphyrin (ZPP, the form of EP in red blood cells) was common.[1] Both of these markers reflect essentially the same compound.[1] One of the most sensitive effects of lead exposure is the inhibition of heme biosynthesis (see Figure 1).[20] An elevated EP level is one of the earliest and most reliable indicators of impairment of the biosynthesis of heme and reflects the average blood lead concentration for the previous four months.[1] Lead inhibits the reduction of iron (III) to iron (II), which allows zinc (II) to be inserted into protoporphyrin by the enzyme ferrochelatase (Zinc competes with iron for insertion into protoporphyrin).[15,20] EP has the benefit of needing only a fingerstick and the cost is not prohibitive. However, the results correlate only with blood lead levels greater than 25 µg/dl.[1,3,15,20,50] Therefore, since the CDC lowered the threshold value for lead poisoning, this test is no longer adequate for screening.

Succinyl-CoA + Glycine

↓

↓ ALA Synthase (Lead can increase this)

5-aminolevulinic acid (ALA)

↓

↓ Porphobilinogen Synthase (Lead can inhibit this)

Porphobilinogen

↓

↓ Porphobilinogen Deaminase

Hydroxymethylbilane

↓

↓ Uroporphyrinogen Synthase

Uroporphyrinogen III

↓

↓ Uroporphyrinogen Decarboxylase

Coproporphyrinogen III

↓

↓ Coproporphyrinogen Oxidase

Protoporphyrinogen IX

↓

↓ Protoporphyrinogen Oxidase

Protoporphyrin IX

↓ (Lead inhibits reduction of Fe^{+3} to Fe^{+2})

↓ Ferrochelatase + Fe^{+2} (or $+Zn^{+2}$)

Heme (Zinc Protoporphyrin)

Figure 1: Biosynthesis of Heme (adopted from Nuttall[20]).

Currently, the test of choice is whole blood lead analysis.[1,3] This is due to detection limits of less than 1 µg/dL, depending on the methodology used. Because lead is incorporated into the red blood cell, an anticoagulant is needed.[15] Heprin has been used in the past, but it is not recommended because microclots can form after two to three days.[15] Special tubes are available for trace metal testing, but for most purposes, standard purple top tubes, with EDTA as the anticoagulant are adequate.[15]

Two current methods are available for the collection of blood lead. The first is venous collection. The major advantage of venous lead is the reduced amount of exogenous lead contamination.[1,3] Venipuncture has also been demonstrated to be less expensive due to the limited number of repeat analysis required.[50] However, venipuncture is often difficult and time consuming, especially on younger children.[51] This is a possible deterrent to screening.[51]

Microcollection by fingerstick is popular for an number of reasons. For the phlebotomist, fingersticks are often much easier to obtain than venous specimens. For the parent, a fingerstick is often viewed as less invasive.[52,53]

The majority of all microspecimens for lead are collected into 500 µL EDTA capillary collection tubes. Filter paper analysis is also available and gaining in popularity.[54] This technique requires only a few drops of blood and the filter paper is stable for six months.[54] More research has been performed on capillary specimens, therefore, it will be discussed in this section. However, the same principles apply to both.

The CDC has called for more research on capillary specimens, which the scientific community has done. A capillary sampling protocol was also issued by the CDC but not endorsed as definitive.[3] It has been reported that up to 50% of all capillary samples show contamination.[31] With this in mind, several rules must be applied to capillary collections. First and most importantly, the capillary specimen is only as good as the blood collection technique and adherence to that technique by the collector.[6,15] Second,

no capillary sample should be considered definitive because there will always be a chance of contamination.[6] Most current studies indicate a positive bias for capillary samples when compared with venous lead results, although falsely lowered capillary values have also been noted.[14,55] Gross contamination, although not prominent, is still found in most studies and in the field. However, handwashing with alcohol prewipe, alcohol prewipe alone, and other devices have been found to be effective in removing most external contamination.[14,46,51,53,55,56,57,58,59,60] Other studies have also found that when children who have elevated capillary results return for venous confirmation, the lead values are much lower, indicating gross contamination.[14,53,58] However, not all studies find this to be the case.[14,57] One study found that repeat capillary analysis, after initial capillary analysis, showed almost the same decrease as a venous repeat.[14] This indicates that some other factor may be responsible for the decrease. In another study, an instant venous confirmation was performed on elevated capillary and filter paper results. The instant confirmation values were compared to a thirty day venous confirmation.[56] The results showed an instant false positive rate of 13.5 % for capillary and 19.1% for filter paper. The corresponding 30-day false positive rate was more than double for both, 31.3% for capillary and 46% for filter paper. These findings suggest that day to day lead fluctuations may cause a perceived higher false positive rate than actually exists. Appendix B lists the major studies on capillary samples since 1974.

The definitive method for lead analysis is isotope dilution mass spectrometry.[1,15] This method is not of practical use for the clinical laboratory. The most common methods are atomic absorption spectrometry (AAS) and anodic stripping voltametry (ASV).[1,15] AAS with a graphite furnace provides excellent sensitivity and is very accurate. Limitations include matrix effects, low throughput, long sample preparation times, and high cost.[1,15,54]

ASV is cheaper to perform, both in supplies and instrumentation.[15,54] However, this method is slow and the sensitivity of the instrument is hard to maintain.[54] Results can be quantitated down to 5 µg/dL, although variability exists on all results less than 15 ug/dL.[54] Laboratories who use this method generally have higher coefficient of variations on College of American Pathologists (CAP) proficiency surveys.[15] CAP surveys show that 10 to 20 % of those labs using AAV or AAS do not meet the proficiency standards of 4 µg/dL.[46] This permissible variation and frequency of inaccuracy may result in faulty advice for values less than 20 µg/dL.[46]

Inductively coupled plasma - mass spectrometry (ICP-MS) has been used in the past in the environmental industry.[62] It is now becoming more common in clinical labs.[15,18] The procedure requires minimal specimen preparation time, provides outstanding sensitivity and specificity, high throughput, and the cost per test can be quite low, provided an adequate volume of specimens.[15,18] The disadvantages of ICP-MS are the complexity and initial cost of the instrumnet.[15] In the future, sources of lead poisoning can potentially be identified by ICP-MS using lead isotopes.[15,18] This technology is definitely the method of choice for laboratories performing large volumes.

Treatment of Lead Poisoning

Table 1 lists the CDC recommendations for interpretation of blood lead results and follow up activities. Those children in classes III, IV, and V may need pharmacologic treatment.[3] There are four chelating agents used in the treatment of lead poisoning. They are D-pencillamine, edetate disodium calcium (CaN_2 EDTA), dimercaprol (BAL), and succimer (DMSA).[1,8,15,60,61,62] Chelation is not recommended at levels less than 25 µg/dL.[6] Levels between 25 and 45 µg/dL constitute a gray area and different practices abound. There has been no solid proof of cognitive improvement after chelation therapy.[6] Although chelation does reduce blood lead, it should not be substituted for identifying the lead source and removing it.[1,3,6] Succimer was approved

Table 1

CDC Recommendations for Elevated Blood Lead Management

CDC Class	Lead Concentration(μg/dL)	Action/Comment
I	<10	Not considered to be lead poisoned. No rescreen necessary.
IIA	10-14.9	Possibility of lead poisoning. If many children in the community are in this level, interventions by appropriate agencies may be necessary. Children under three in this class should be rescreened every 3 to 4 months until 2 consecutive measurements are < 10 or 3 are < 15 μg/dL. If the child is high risk, as determined by questionnaire, rescreening should continue once a year. No pharmacologic treatment needed.
IIB	15-19.9	Possibility of lead poisoning. Environmental investigation and evaluation should be performed, if the level is persistent. All children should be rescreened at 3 to 4 months. Parents should be educated. If test was a capillary puncture, then rescreening should be accomplished within 1 month. No pharmalogic treatment needed.
III	20-44.9	Probable lead poisoning. Rescreen as soon as possible. If test was a capillary puncture, retest within 1 week. Environmental evaluation and remediation are necessary. Possible pharmacologic treatment.
IV	45-69.9	Medical treatment and environmental assessment within 48 hours. Rescreen within 48 hours. Probable pharmacologic treatment.
V	>70	Medical treatment and environmental assessment should begin immediately.

Adapted from CDC[3]

in 1991 by the Federal Drug Administration. It is the only chelator that is administered orally.[15] Although superior to the other available drugs, some surveys have found that it is used less than one third of the time. The same study found that the knowledge of pediatricians is weak in the areas of lead exposure and poisoning, including the level of toxicity, sources of lead, effects of lead poisoning, and treatment.[13] However, these findings could be disagreements with the CDC recommendations.

MATERIALS AND METHODS

Distribution of Capillary and Venous Lead Values

Lead result logs (from Associated Regional University Pathologists, Salt Lake City, Utah) were reviewed. The ages of the patients reviewed ranged form 6 months to 6 years. The dates reviewed were from October 1993 to June 1994. The patients were classified as either having a venous sample or a capillary sample. Descriptive statistics were performed for both venous results and capillary results.

Analysis of Elevated Lead Followups

Selected patients, with elevated venous or capillary blood lead results were followed for four months. This was done to determine if these patients were followed according to CDC recommendations and to compare values of repeat to initial analysis.

Soil-Lead Mixture Preparation

Lead, 200 mesh and finer, manufactured by Spectrum Chemical Corporation, Gardena CA, was obtained from a commercial vendor (The Chemical Shop, Centerville UT). Soil was obtained from a freshly plowed suburban garden (330 N 1000 E Kaysville UT). The lead was mixed with soil at approximately a 1:12 ratio. The resulting mixture was analyzed for lead content at a certified environmental testing laboratory (Rocky Mountain Geochemical Corporation, West Jordan, UT). The lead-soil mixture was measured at 7.90% lead.

Recruitment of Volunteers

Volunteers were solicited by Captain Nathan Johnson and Senior Airman Craig Woodall at the 649th Medical Group Hospital, Hill Air Force Base Utah. Thirty volunteers were solicited. Each received and signed a consent form approved by the University of Utah Medical School Institutional Review Board. Volunteers received no compensation, other than knowledge of their lead values.

Collection of Specimens

Venous specimens were collected in the normal manner. Capillary and filter paper specimens were collected using a modified ARUP method. Appendix C lists this collection procedure. Collection of all specimens was performed by an accomplished phlebotomist, Senior Airman Craig Woodall.

Preparation and Analysis of Samples

Samples were prepared in the ARUP metals laboratory using established operating instructions. Appendix D lists the sample preparation steps for venous, capillary, and filter paper specimens. All samples were quantitated on an ICP-MS (Elan 5000, Perkin-Elmer). Testing was performed on the same day to eliminate day to day analytical variability.

Statistical Evaluation

Statistical evaluation was accomplished by the use of NCSS, a computer program written by Dr. Jerry Hientze (Kaysville UT). Differences between the large capillary and venous databases were determined by use of pooled variance T-tests. Differences between followup tests and handwashing experiments were determined by use of paired T-tests.

RESULTS

Distribution of Capillary and Venous Lead Values

Over 5,100 venous and 1,100 capillary samples were reviewed. The mean (3.83 µg/dL) of the venous samples was statistically less ($p < .0005$) than the mean (4.61 µg/dL)of the capillary samples. The difference between the mean values, the theoretical contamination, was 0.78 µg/dL. Although a larger percentage of venous specimens were in CDC group I (0-10 µg/dL), the percentage of values in group III and higher (greater than 15 µg/dL) was equal (1.5% for both). Figure 2 is a representation of the cumulative percentage of each group. Seasonal variation was also seen in both groups. Figure 3 shows this combined seasonal variation from October 1993 to October 1994. A comparison is also made to the seasonal variation seen in the Minnesota study.[38]

Analysis of Elevated Lead Followups

Appendix E provides a summary of elevated capillary and venous repeats. Each group of initial results is statistically different from the repeat results, although the mean difference for capillary results is much higher.

Effect of Handwashing in Eliminating Gross Contamination

Venous, capillary, and filter paper specimens were collected (see Appendix E). Table 2 lists the results of the 30 samples. Summary statistics for each group are listed in Table 3. Statistical analysis revealed significant differences between venous and capillary handwashing ($p=.045$), venous and capillary non-handwashing

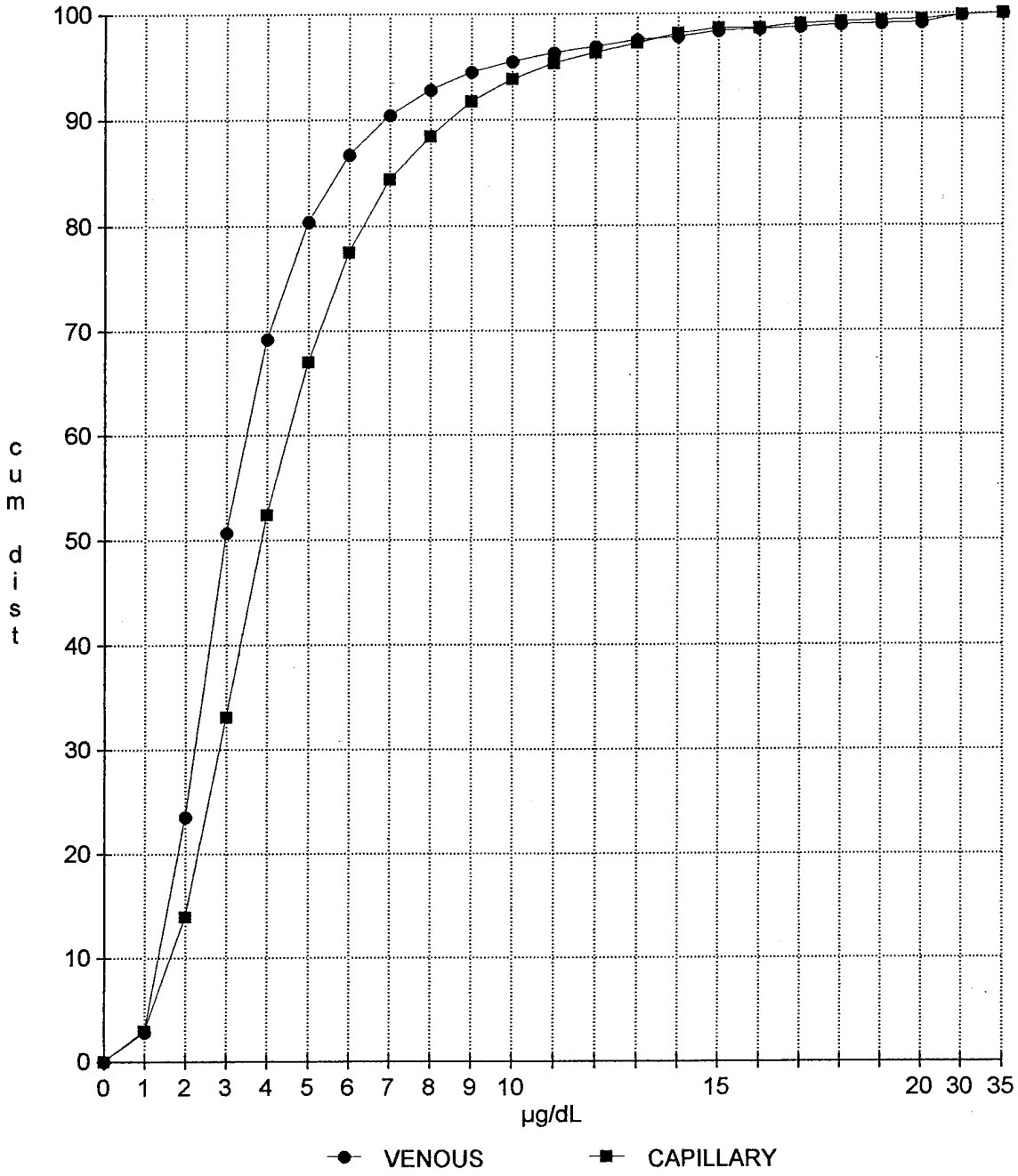

Figure 2: Cumulative Distribution of Venous and Capillary Samples

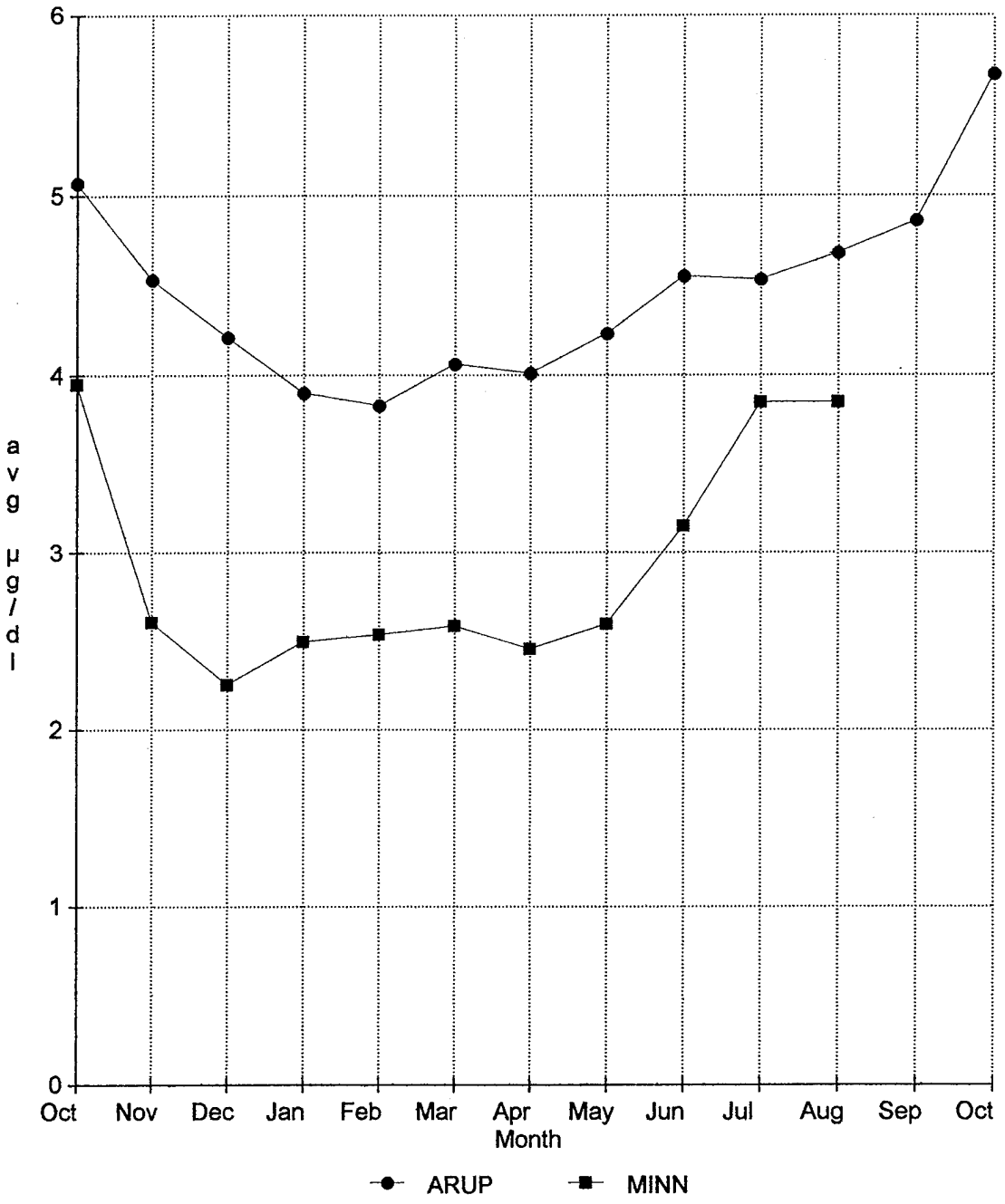

Figure 3: Comparison of Seasonal Variation

Table 2

Handwashing Effects on Capillary and Filter Paper Specimens

Specimen #	Venous	Capillary (Handwash)	Capillary (No Handwash)	Filter Paper (Handwash)	Filter Paper (No Hashwash)
1	0.84	1.48	88.9	2.67	19.4
2	0.75	1.63	25.0	4.98	3.40
3	1.10	1.40	7.15	2.11	0.00
4	1.12	1.88	1.83	4.43	0.30
5	2.17	42.8	493	4.81	18.5
6	1.96	17.8	1170	10.1	27.3
7	0.82	1.23	58.1	2.59	1.39
8	0.78	1.30	79.1	8.20	1.07
9	2.36	3.80	32.2	4.50	13.7
10	2.18	5.50	469.6	4.00	5.30
11	2.63	4.03	385.8	3.70	2.78
12	2.11	3.70	111.8	40.5	4.19
13	0.78	3.20	10.3	14.9	2.83
14	0.92	1.03	41.6	12.4	0.31
15	0.80	2.15	229	0.00	0.98
16	1.08	2.28	39.2	5.70	4.99
17	1.17	9.75	4.33	4.50	1.26
18	1.48	1.98	154.1	9.20	0.71
19	0.76	1.40	52.9	0.60	44.7
20	0.86	1.13	28.3	2.80	1.38
21	0.98	1.05	18.8	1.30	0.72
22	0.86	3.28	1182	1.00	0.00
23	1.15	1.73	112	9.60	0.72

Table 2 (Continued)

Specimen #	Venous	Capillary (Handwash)	Capillary (No Handwash)	Filter Paper (Handwash)	Filter Paper (No Hashwash)
24	1.30	1.48	22.4	0.30	0.71
25	1.15	2.43	9.60	4.90	0.32
26	1.94	1.90	109	2.60	6.40
27	1.86	2.18	30.4	1.33	97.2
28	1.07	1.20	45.7	2.80	1.53
29	1.01	1.28	33.3	7.40	0.16
30	0.96	1.93	11.8	5.50	1.52

All results are in µg/dL.

Table 3

Summary Statistics

Variable	N	Mean(µg/dl)	Std Dev	C.V.	Range	100%tile	75%tile	50%tile	25%tille	0%tile
V	30	1.30	0.56	43.0	1.88	2.63	1.86	1.09	0.86	0.75
C-1	30	4.27	8.00	187	41.7	42.8	3.28	1.92	1.40	1.03
C-2	30	169	304	180	1180	1180	112	43.7	22.4	1.83
F-1	30	5.98	7.46	125	40.5	40.5	7.40	4.47	2.59	0.00
F-2	30	8.79	19.4	221	97.2	97.2	5.30	1.46	0.71	0.00

V=Venous
C1=Capillary + Handwahsing
C2=Capillary with no Handwashing
F1=Filter Paper + Handwashing
F2=Filter Paper with no Handwashing

(p=.005), venous and filter paper handwashing (p=.001), venous and filter paper nonhandwashing (p=.041), and capillary handwashing and nonhandwashing (p=.006). No statistical difference was found between filter paper handwashing and nonhandwashing (p=.485).

DISCUSSION

When addressing the question of the adequacy and appropriateness of capillary specimens, several issues should be examined. One issue is the continuing debate over capillary sampling methodologies. Contamination will never be completely eliminated. Some now believe that any lead is potentially dangerous to children. If that is true, then any contamination will further exacerbate the results. Contrast this to the current CDC cutoff for possible lead poisoning at blood lead levels greater than 10 µg/dL. Under this system, any lead result under 10 µg/dL is considered acceptable. Therefore, at levels under 10 µg/dL, lead contamination is not an issue.

Another way to examine contamination is to look at the past. Appendix A lists some of the major surveys that reveal how much lead levels have dropped in the past 30 years. Thirty years ago, it was common to have a considerable percentage of children with lead levels above 25 µg/dL. Twenty years ago, the average adult lead level, which historically has been less than child levels, was 16 µg/dL. Today, most studies find the average child to have levels less than 4 µg/dL. This dramatic decrease in lead levels has two important impacts on the credibility of capillary samples. First, because lead levels dropped, so too has the importance of contamination. For example, if the average lead value was 9.5 µg/dL and the average contamination was 2.0 µg/dL, it is easy to see why many samples would be above the cutoff level of 10 µg/dL. However, with current averages around 4.0 µg/dL, contamination is not as big an issue. Second, with the decreasing levels of

lead in the environment, a corresponding drop in the amount of contamination is also inevitable.

There are two types of contamination that can occur, major or "gross" contamination and minor contamination. Each is important and will be discussed. Gross contamination is listed in the literature as being a major deterrent to capillary methodologies. In the past, there is no doubt that capillary contamination of specimens was present and affected many samples. However, with much lower lead levels the environment, it may play a lesser role. Most studies that look for gross contamination will find it, although small in percentages. There is evidence to suggest that day to day fluctuations in lead levels constitute a major portion of the decrease seen at retest. This day to day fluctuation would seem to the provider to be evidence of contamination. This is exacerbated by the scrutinization that elevated capillary values receive. Appendix E is an analysis of followup lead testing of elevated results taken from the ARUP database, capillary and venous. This analysis shows a statistically significant difference between the means of repeat capillary and venous and their corresponding initial results. Every capillary and 89% of venous repeats were lower than initial results indicating the major role day to day fluctuations may play. Seasonal and instrumental variation may also be present. The difference in means is greater in capillary than venous samples which probably means that in capillary samples, both fluctuations and contamination played a part. Some examples of gross contamination are obvious, such as one seen that had an initial result of 35 µg/dL and a repeat within 7 days of 3 µg/dL.

Analysis of a large database of venous and capillary results could demonstrate if gross contamination, minor contamination, a mixture of both types of contamination, or no contamination is present. Table 4 lists the data for this section (also refer to Figure 2 for a graphic depiction). It is apparent by visual examination of the data, the percentages greater than 5 and 10 µg/dL, that some

Table 4

Venous and Capillary Database Summary

	Venous	Capillary
N	5129	1164
Mean (µg/dL)	3.83	4.61
% > 5.0 µg/dL	18.4	29.7
% > 10.0 µg/dL	3.9	5.9
% > 15.0 µg/dL	1.5	1.5
Theoretical Contam (µg/dL)	N/A	0.78
CDC Group I (%)	96.1	94.1
Theoretical Group I (%)	95.9	95.3
CDC Group IIA (%)	2.4	4.4
Theoretical Group IIA (%)	2.6	3.3
CDC Group IIB (%)	0.7	0.6
Theoretical Group IIB (%)	0.7	0.6
CDC Group III (%)	0.8	0.9
Theoretical Group III (%)	0.8	0.8

Capillary Theoretical = Actual Results - Theoretical Contamination (if uniform contamination, simulates venous results)

Venous Theoretical = Actual Results + Theoretical Contamination (if uniform contamination, simulates capillary results)

type of contamination occurred resulting in a higher percentage of capillary specimens in CDC group II. The percentage greater than 15 µµg/dL is the same for both capillary and venous. This indicates that gross contamination is not a major problem, but still occurs. Therefore, minor contamination is the area of concern.

Two types of minor contamination can occur. First, there can be uniform contamination where all samples have equivalent amounts of contamination. Second, there can be variable contamination, where some samples receive quite a bit and others receive none at all. If uniform contamination occurs, then a "theoretical" contamination rate could be calculated by subtracting the mean of venous samples from the mean of capillary samples in a database of results. In this case, the difference is 0.78 µg/dL. If this theoretical contamination is correct, it could be added to all the venous results in the database. For example, a venous result of 9.0 µg/dL would become 9.78 µg/dL. In this manner, all the venous results in the database would simulate capillary results. The same method can be applied to make capillary results simulate venous results by subtracting theoretical contamination from all capillary results. After addition of this theoretical contamination rate to venous specimens, the percentages of venous and capillary results in each CDC grouping were compared. If uniform contamination occurred, the percentages would be the same. However, the percentages are different, although closer together. This suggests that variable contamination is responsible. This is also supported by the fact that some capillary results were quite low with the percentage of results in the 0.0 - 1.0 µg/dL range lower for capillary than for venous. This indicates that little or no contamination occurred in these samples.

A minor area of concern in regard to capillary testing is the lack of provider compliance to government recommendations. In order for capillary testing to be used in practice, results and followup should be no harder to use than venous testing. Appendix F lists the results of analysis of the question, "Are CDC

recommendations being followed?" It should be noted that providers who had followup testing done at a laboratory different than ARUP could skew these results, but this is probably a rare occurrence. The answer for the majority of patients is no, recommendations are not being followed. The CDC recommendations are mildly confusing at best due to different screening recommendations for each CDC group, children broken up into ages 0-3 and 3-6, and different rules for followup of capillary results, etc. However, there appeared to be no major difference between provider followup to venous and capillary specimens. It has been reported that many providers disagree with the CDC and many more are ignorant of major components of the recommendations Therefore, provider compliance to these recommendations should play no role in recommending venous over capillary.

As mentioned in the introduction section, the major advantage to capillary testing is the ease of collection. It is no coincidence that skilled pediatric phlebotomists are very sought after and valued by clinical laboratories. Even the most skilled pediatric phlebotomist can find obtaining a venous specimen from a small child difficult. Capillary specimens, as a general rule, are much easier to collect and less traumatic to parent and child. Capillary samples are harder to work with in the laboratory setting and do not offer the volume of blood often necessary for repeat analysis. However, this should not limit capillary use.

The main issue remaining concerning capillary samples is the fact that gross and significant minor contamination, which can move a child from a lower CDC group to an elevated group, still occurs. Many methods have been tried to alleviate this problem (see Appendix B). Differing results have been found, but as a rule, proper handwashing seems to eliminate most lead contamination in the field Some studies find that use of an alcohol wipe alone does this. Of the studies examined, only one introduced external contamination (1% lead soil).[54] However, no handwashing was performed in this study (alcohol wipe vs. barrier method).

Soil around lead smelters have been found to contain as much as 7% lead. Therefore, this was the goal for the lead soil mixture in this experiment. The concentration turned out to be 7.94%. Samples were collected as mentioned in Appendix C. The results of this experiment are listed in Table 2. This experiment clearly indicates that proper handwashing and meticulous attention to detail by the phlebotomist can reduce extremely gross contamination to manageable levels. The mean of capillary handwashing specimens was 4.61 µg/dL, compared to over 168 µg/dL for nonhandwashing specimens. This difference was statistically significant ($p=.045$). The venous baseline was 1.30 µµg/dL. Of the 30 volunteers, 28 came from white collar hospital employees. However, two came from a machinist shop. The phlebotomist noted that the hands of the machinists looked dirty, even after proper handwashing. The two machinists had capillary handwashing results of 42.8 and 17.85 µg/dL and nonhandwashing results of 492.5 and 1172.0 µg/dL. This may have affected this study, but this problem should not occur in children. As can been seen in Table 2, filter paper results were sporadic and most likely indicate a flaw in the design of this study. Filter paper specimens were collected at the same time as capillary specimens. In retrospect, they should have been collected before the capillary specimens. This resulted in a dilution effect, whereby most of the introduced lead was gone by the time the filter paper specimen was collected. Also, due to the new nature of this procedure, matrix effects may have occurred. Nevertheless, this study clearly demonstrates the effectiveness of handwahisng on capillary samples.

The last item of note applies to all lead testing. Little in the literature speaks of the effect that seasonal variation has on screening. However, it is a known phenomenon (see Figure 3) and accepted fact, although no consensus has been reached on why it occurs. The CDC has set forth stringent guidelines for lead testing. This fact, combined with the fact that significant variation is allowed for

methodologies (the before mentioned high coefficient of variations for AAS and ASV), the day to day variation of lead, and seasonal variation, demonstrates why results can vary so widely. Some form of standardization needs to exist beyond proficiency testing. If lead is 40% higher in summer than in winter, how can the same cutoff be applied to both time periods? This current ludicrous practice would be similar to assigning a fasting glucose the same value as a glucose a few hours after a meal. There are no simple answers to this problem. For example, day to day fluctuations will not stop, different levels of seasonal variation occur in different areas , etc. More research needs to be done to assess the impact these factors have on screening.

In conclusion, the adequacy of capillary lead samples is not an easy or simply quantitative answer. There will never be a 100% correct answer. Thirty years ago, even with the large amount of external contamination, there was no 100% correct answer. However, the bodies of evidence, including this thesis, indicate that it is an acceptable screening mechanism, if the proper guidelines are followed.

APPENDIX A

LEAD LEVEL SURVEYS

DATE(s)	AUTHOR	FINDINGS
1965	Chicago Board of Health[5]	5 to 15% of children screened had blood lead values greater than 50 µg/dL.
1971	Sayre,Charney,et al.[1]	In an inner city study in Rochester New York, 37% of children had blood lead values greater than 40 µg/dL.
1974	CDC[7]	4.8% of children (7.6% of blacks) have blood lead levels greater than 40 µg/dL.
1976-80	Annest[3,11]	Between 1976 and 1980, the use of leaded gasoline was cut in half. During this same time the average blood lead declined from 16 µg/dL to less than 10 µg/dL.
1976-1980	NHANES II[8]	The average blood lead in the United States was 12.8 µg/dL (for children ages 1 to 5 the values were 13.7 µg/dL for whites and 20.2 µg/dL for blacks). The percentage of children greater than 10 µg/dL was 85% for whites and 97.7% for blacks.
1984	ATSDR[3,63]	17% of American preschool had blood lead levels greater than 15 µg/dL. 4.4 million women (of child bearing age) are estimated to have blood lead values greater than 10 µg/dL.

DATE(s)	AUTHOR	FINDINGS
1988-91	NAHNES III (phase I)[8,64]	8.9 % (1.7 million) of U.S. children had blood lead levels greater than 10 µg/dL. The average blood lead in the U.S. was 2.8 µg/dL (3.2 and 5.6 µg/dL for white and black children, respectively). The percentage of children with levels greater than 10 µg/dL was 5.5% for white and 20.6% for black children.
1968-88	City of Chicago Dept Dept of Health[11]	For children(ages 6 months to 5 years), the average blood lead level dropped from 30 to 12 µg/dL (from 1968 to 1988) and the decline was strongly associated with declining air lead levels.
1988	ASTDR[51]	16% percent of U.S. children had lead levels greater than 15 µg/dL (this information used in 1994 article).
1980s	EPA[1]	During the 1980s, the average blood lead level dropped from 17 to 4-6 µg/dL.
1990	EPA[14,24]	3 million children in the U.S. have levels greater than 10 µg/dL.
1991-92	Nordin, Rolnick et al.[39]	2.5% of children (ages 9 months - 2 y years) enrolled in a suburban HMO had lead levels greater than 10 µg/dL.

DATE(s)	AUTHOR	FINDINGS
1992	NHANES III[1]	Less than 1% of U.S. children have blood lead values greater than 25 µg/dL.
1992	U.S. Dept of Health[6]	The blood lead of children was 4 - 6 µg/dL.
1992	California Dept of Health Services[44]	More than 200,000 children living in poverty were tested. Less than 0.3% had lead levels greater than 20 µg/dL.
1992	Binns, Le Baily, et al.[14]	At a suburban Chicago clinic, 2.1% of 1,393 children had lead levels greater than 10 µg/dL. None had levels greater than 30 µg/dL.
1992-93	Norman, Bordley, et al.[60]	20,720 North Carolina children ages 6 months to 6 years had blood lead levels determined. 20.2% were greater than 10 µg/dL, 3.2% were greater than 15 µg/dL, and 1.1% were greater than 20 µg/dL. The levels in rural areas were slightly less than urban areas.
1992-94	U.S. Army[65]	3.17% of U.S. Army dependents (ages 6 months to 6 years) had blood lead levels greater than 10 µg/dL.
1992-94	U.S. Navy[65]	2.13% of U.S. Navy dependents (ages 6 months to 6 years) had blood lead levels greater than 10 µg/dL.

DATE(s)	AUTHOR	FINDINGS
1992-94	U.S. Air Force[65]	0.87% of U.S. Air Force dependents (ages 6 months to 6 years) had blood lead levels greater than 10 µg/dL.
1992-94	Department of Defense[65]	1.94% of DOD dependents ages 6 months to 6 years) had blood lead levels greater than 10 µg/dL.
1993-94	Nathan Johnson (unpublished)	Of 5,129 venous samples (ages 0 -6 years), 82.6% were below 5 µg/dL, 96.1% were below 10 µg/dL, and 98.5% were below 15 µg/dL. The mean was 3.8 µg/dL.
1993-94	Utah Dept of Health (unpublished)	Of 1,610 Medicaid eligible children in Utah, 96.6% had lead levels less than 10 µg/dL, 98.9% were less than 15 µg/dL, and 99.5 were less than 20 µg/dL. No child had a value greater than 25 µg/dL. The mean was 3.7 µg/dL.

APPENDIX B

CAPILLARY LEAD SPECIMEN SURVEYS

DATE(s)	AUTHOR	FINDINGS
1974	Mitchell[51,53]	24 children had venous and capillary (with collodion spray) lead samples drawn at the same time. The mean of the venous and capillary differed by 1.80 g/dL (with means of 24.88 and 23.08 µg/dL for venous and capillary). 22 to 29% of capillary samples were found to be falsely elevated.
1984	Sinclair, Dohnt[56]	154 paired venous and capillary were analyzed. 5 samples showed gross contamination. Of the remaining 149 samples, there was a small, but statistical difference. Capillary samples were collected using soap and alcohol wipes.
1991-93	Schlenker[59]	Of 300 paired venous and capillary specimens (with 4 different cleaning methods), only 1 sample had gross contamination. These specimens were collected in the field. The difference between the samples were negligible.
1992	McGregor, Jones[58]	A positive bias of 1.8 µg/dL was demonstrated for capillary specimens. Of 202 children with paired venous and capillary specimens, there were no false negatives and 15 false positives for the capillary specimens.

DATE(s)	AUTHOR	FINDINGS
1992	Schonfeld, Allen[57]	At mass screenings, some elevated lead values were repeated immediately, and some were recalled at 30 days. The immediate false positive rate for capillary and filter paper were 13.5% and 19.1%. The corresponding false positive rates for 30 days were 31.3% and 46%. This suggests that day to day variations in lead levels may cause providers to perceive high false positive rates.
1992	Binns[14,46]	1296 capillary specimens were collected. 47 (3.6%) were greater than 10 µg/dL. On repeat analysis, 15 (32%) were >10 µg/dL. 85% of venous repeats were less than initial capillary analysis, and 15% were greater than initial capillary analysis.
1992-93	Norman, Bodley[60]	580 children with capillary lead values > 15 µg/dL were retested (some venous and some capillary). Venous repeats were 5.4 µg/dL less, whereas capillary repeats were 4.8 µg/dL less.
1993	Sargent[55]	Hands of 29 adults were contaminated with 1% lead. A barrier technique demonstrated good correlation with the venous sample, whereas alcohol cleansing alone was poor in eliminating lead.

DATE(s)	AUTHOR	FINDINGS
1993-94	Nathan Johnson (unpublished)	Lead values of a large number of venous and capillary specimens showed a small, but statistical difference in the means (3.83 µg/dL for venous and 4.61 µg/dL for capillary).
1995	Nathan Johnson (unpublished)	Hands of 30 adults were contaminated with 7.9% lead. Handwashing with alcohol pre-wash removed most lead, whereas alcohol alone left many samples with gross contamination.

APPENDIX C

COLLECTION OF SAMPLES

Capillary and Filter Paper Collection Procedure

STEP 1: Explain the procedure to the volunteer. Have the volunteer read and sign the consent form. If the volunteer would like to know his/her lead level, have the patient include address/or phone number on the consent form. Log the patient onto the log provided.

STEP 2: Set up all supplies and equipment. **IMPORTANT** - Keep lead-soil mixture at least fifteen feet away from procedure site (to avoid contamination).

STEP 3: Wash hands well before handling supplies and equipment. Keep all supplies in a clean plastic box with snap lid, a zip-lock baggie, or in their original container..

STEP 4: Put on gloves and eye protection.

STEP 5: Collect a routine venipuncture (at least 5 mL) into EDTA tubes. Label the specimen as follows:

1-VNJ8219

1=PATIENT # FROM THE LOG (will be from 1 to 30) V=VENIPUNCTURE, NJ = INITIALS OF VOLUNTEERS, 8219=LAST 4 SSN.

STEP 6A: Collect non-handwashing specimens. Determine the finger to collect specimen from. Have volunteer wash his/her hand. Proceed to the area where the lead-soil mixture is. Have the volunteer "dip" the finger into the lead-soil mixture (enough to cover the finger). The soil/lead mixture is located in the "red top" tube. Proceed back to collection area.

STEP 6B. Wash your hands. Put on gloves. Rinse off powder, dry with paper towel. Place a clean paper towel on the collection table. Obtain filter paper from zip lock bag. Place on clean towel (handle filter paper in the area below the line). See figure 4.

STEP 6C. Clean the contaminated finger with two alcohol pads (being careful not to contaminate the filter paper). Dry with a clean gauze pad. It is very important to keep the finger isolated from the rest of the hand.

STEP 6D. Lance the lateral portion of the finger. Avoid getting too close to the nail bed. Apply slight pressure to the finger to start blood flow. Quickly wipe away the first drop of blood (which contains excess tissue fluid). Keep the finger in a downward position to increase blood flow. After wiping away the first drop, hold the finger above the filter paper and allow two separate drops of blood to fall in **TWO** separate spots on the discs upper surface. At least two dime size spots are required. After this has been completed, collect a capillary specimen. If at all possible, fill the microtube to the line (500 uL). As a minimum, fill it up at least half way. Avoid clots. Allow the filter paper to dry in special device for one hour. Then return to ziplock bag.

NOTE: You will be drying a minimum of 2 filter paper specimens at the same time.

MAKE SURE you can identify one from the other (VERY CRUCIAL). This could be done by marking 1H (specimen #1 handwashing) or 1N (specimen#1 nonhandwashing) on the area allowed to be handled.

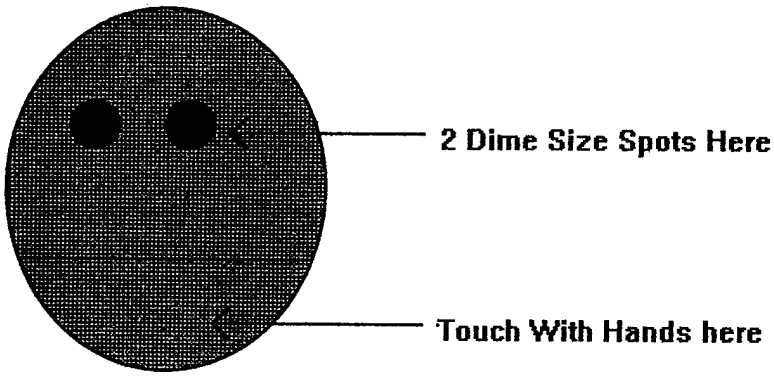

Figure 4. Proper collection site for filter paper.

ZIPLOCK BAGGIE: 1- FNHWNJ8219

1=NUMBER FROM LOG F=FILTER, NHW=NO HAND WASHING,

NJ=INITIALS, 8219 = LAST 4 SSN

CAPILLARY SPECIMEN: CNHWNJ8219

1= NUMBER FROM LOG C=CAPILLARY, NHW, NJ, 8219 = SAME AS

ABOVE

STEP 7: Collection of Handwashing specimens. Follow the same directions as in Step 6 with the following exceptions.

In step 6C, have the ***volunteer first wash hands***, then dry them. Put some soap on a gauze, and you clean the finger yourself. Then proceed to with the alcohol pads etc.... as in step 6C. THIS STEP IS CRUCIAL TO THE EXPERIMENT.

Labeling: ZIPLOCK BAGGIE: 1-FHWNJ8219 HW=HANDWASING

CAPILLARY: 1-CHWNJ8219

After completion, each volunteer should have 5 specimens:

1 Venous

2 Capillary (1 handwashing, 1 nonhandwashing)

2 Filter paper specimens with 2 drops (1 handwashing, 1 nonhandwashing)

Put each specimen into a small zip-lock bag (for the filter paper, you can use the ones that they came in) and then put the five small bags into one larger one. Label on the outside of each small bag the specimen number.

APPENDIX D

PREPARATION OF SAMPLES

Specimen Preparation

Blood

1. Label a 10 mL polypropylene tube for each sample.
2. Label a 16 x 100 mm glass tube for each whole blood sample.
3. Dispense 0.5 mL of 1000 µg/L Yttrium standard into each tube.
4. Pipette 0.5 mL of each sample into appropriate tube.
5. Vortex.
6. Add 4.0 mL of deionized water to each tube, cap, and mix well.
7. Centrifuge the glass tubes at 2500 RPM for 5 minutes.
8. Decant the supernatant through a screening column into testing tube.

Filter Paper

1. Label a 10 mL polypropylene tube for each sample.
2. Label a 16 x 100 mm glass tube for each whole blood sample.
3. Place one punch (disc) from one spot of the absorbent paper in the glass tube.
4. Dispense 0.5 mL of EDTA solution into each glass tube. Let sit for 10 minutes.
5. Vortex. Let sit for another 10 minutes
6. Pipette 1.0 mL of the 10 µg/L Yttrium standard into each tube. Mix well.
7. Centrifuge the glass tubes at 2500 RPM for 5 minutes.
8. Decant the supernatant through a screening column into testing tube.

APPENDIX E

ANALYSIS OF FOLLOW-UP LEAD TESTING

Capillary lead results and their resulting follow ups are compared against Venous lead results (which are split into 10-15 and >15 µg/dl). This split is due to the fact that in the >15µg/dl (Venous only), education, abatement, and possible chelation could possibly affect results (should not affect 10-15). Results were taken from both the high and low seasonal months to limit effect of seasonal variability.

CAPILLARY RESULTS:

N=16	<10	10-15	15-20	>20
Initial	NA	5	2	9
Repeat	9	6	0	1

Paired T-Test : P=<.0001
Mean Diff: 11.81 µg/dL
Correlation: .2825
Every repeat result less than original

Venous (10-15 µg/dL)

N=18	<10	10-15	15-20
Initial	NA	18	NA
Repeat	7	10	1

Paired T-Test: P=.0004
Mean Diff: 2.74 ug/dL
Correlation: .4394
15 of 18 repeats lower than original

Venous (>15 µg/dL)

N=18	<10	10-15	15-20	>20
Initial	NA	NA	7	11
Repeat	3	6	3	6

Paired T-Test: P=.0003
Mean Diff: 5.82 µg/dL
Correlation: .7831
17 of 18 repeats lower than original

Summary:
--It is obvious that gross contamination still occurs with capillary specimens
--Why are the great majority of venous repeats lower than original (nutritional counseling, abatement, chelation, etc.)? But why for both venous groups?

APPENDIX F

ARE CDC RECOMMENDATIONS BEING FOLLOWED?

The information comes from the ARUP database of lead from lead (10-93 to 10-94) on children ages 0-6.

The following criteria were used (from CDC):

Classifications: I (<10 µg/dL)
IIA (10-15 µg/dL)
IIB (15-20 µg/dL)
III (20-44 µg/dL)

Children <3: Class IIA - rescreen within 3-4 months
Class II B- rescreen within 3-4 months
Class III - repeat, rescreen within 3-4 months

Children >3: Class IIA - no rescreen necessary
Class IIB - rescreen within 3-4 months
Class III - repeat, rescreen within 3-4 months

CAPILLARY RESULTS:

			Repeated	No Repeat
under 3 years of age:	N=20	Class IIA:	4	8
		Class IIB:	1	0
		Class III:	6 *	1

*(3 not repeated immediately, as suggested)

Total 20, 11 Repeated (55%), 8 repeated per CDC (40%)

3 to 6 years of age:	N=9	Class IIA:	1(unnecessary)	3
		Class IIB:	1	1
		Class III:	3*	0

*(1 not repeated immediately, as suggested)

Total 9, 5 of these need repeated (56%), 4 of these repeated (80%), 3 repeated per CDC (75%), 1 of 4 in Class IIA were unnecessarily repeated (25%).

VENOUS RESULTS:

Under 3 years of age:	N=52	Class IIA:	13	19
		Class IIB:	4	3
		Class III:	6*	7

*(5 not repeated immediately, as suggested)

Total 52, 23 repeated (44%), 18 repeated per CDC (35%)

			Repeated	No Repeat
Ages 3 - 6:	N=52	Class IIA:	5(unnecessary)	21
		Class IIB:	3	11
		Class III:	6*	6

*(4 not repeated immediately, as suggested)

Total 52, 26 need repeating, 17 were repeated (65%), 13 repeated per CDC (50%), 5 of 26 in Class IIA were repeated unnecessarily (19%).

Summary Conclusions:
34 out of 92 leads that needed repeating (37%) were done so per CDC .
6 out 30 leads were repeated unnecessarily (30%).

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