junctions (*16*). The well-known stimulatory effect of CCK-OP injected systemically has been attributed to this direct local action. The present work clearly establishes the presence of a central component.

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## Temporal Trends in the Lead Concentrations of Umbilical Cord Blood

Abstract. *Umbilical cord blood specimens from 11,837 births between April 1979 and April 1981 have been analyzed for lead by anodic stripping voltammetry. The mean was 6.56 ± 3.19 (standard deviation) micrograms per deciliter of blood, and the range was 0.0 to 37.0 micrograms per deciliter. The mean decreased annually by 0.77 ± 0.03 microgram per deciliter, about 11 percent. Lead concentrations were higher in infants born in summer than in infants born in winter (7.17 versus 5.99, probability < .001). A Fourier model of the data is presented, and possible reasons for the decline are discussed.*

As part of a study of the effects on infant development arising from the exposure of a community population to lead, we have examined the blood lead concentrations of a large number of children at birth. Blood lead concentrations have been widely used to assess body burden, and we have used these values to select 250 children for ongoing follow-up study involving environmental and psychological measurements. Secular trends in the blood lead concentrations of pediatric populations may be useful in assessing the impact of certain recently enacted steps designed to decrease community-wide exposure to lead (*1*).

Lead was measured in 11,837 umbilical cord blood samples from the Boston Hospital for Women Lying-In Division from April 1979 through April 1981. This sample represents 97 percent of the live births. This facility serves an ethnically and economically diverse population living in the urban and suburban Boston area. Samples were not included if the mother had hepatitis or if less than 1 ml of blood was obtained. The specimens were collected in a blue-top, heparinized Vacutainer tube (B-D, Rutherford, New Jersey) after the third stage of labor when other blood samples were taken for typing. Typically, 5 ml of blood was recovered. The samples were refrigerated and kept upright during storage, which averaged 3.7 days, before the start of analysis. Samples were processed in batches of 15 in duplicate. Two sonicated aliquots were taken for digestion with a mixture of acids in a vacuum chamber in a modified microwave oven (*2*). Along with each batch of 30 samples, there were five tubes without blood (blanks) to monitor the contamination during the laboratory procedures and two tubes each of standardized pooled blood containing 10 and 20 μg of lead per deciliter of blood. Lead was analyzed by anodic stripping voltammetry (model 2014, Environmental Sciences Associates, Bedford, Massachusetts). The values reported are the averages of two or three determinations.

Contamination during blood collection and handling was found to be negligible. We measured the "fallout" of lead in the delivery suite by leaving two blue-top Vacutainer tubes open for 66 hours; 4 ng of lead was introduced. Also, a syringe assembly was flushed with 0.35 percent perchloric acid and was found to release 2.5 ng of lead in 5 ml. The Vacutainer yielded an amount of lead equal to 0.13 μg $dl^{-1}$ after 1 day of storage with the solution in contact with the stopper and 0.34 μg $dl^{-1}$ after 36 days, most of which came from the stopper. Sonicating and pipetting together introduced less than 0.04 μg $dl^{-1}$. Taken together, these contaminations total less than 0.5 μg $dl^{-1}$ or 10 percent of the average lead concentration. No correction for these effects was applied.

In contrast, contamination by reagents and laboratory ware were not negligible and these values were subtracted from each sample. Acid digestion blanks contributed 3.8 ± 0.2 ng of lead per sample (mean ± standard error of the mean), which would represent 1.9 μg $dl^{-1}$ in the blood, about 26 percent of the detected lead. Since the blanks contributed a sizable and variable amount of lead, we evaluated the coefficient of determination of blanks to daily mean blood level concentrations (linear regression model). We found $r^2 = .0025$ ($r^2$ is a measure of the percentage of variance in the blood lead concentration explained by an independent variable). Thus, 0.25 percent of the variance in the blood values could be attributed to variations in the blank.

Interbatch analytical stability was also assessed for each batch by measurements of the two biological standards. The observed values were 19.79 ± 1.01 and 10.18 ± 0.94 μg $dl^{-1}$ (mean ± standard deviation) for 100 batches. Over time, the standards did not appear to change. Regressing time against the observed concentration yielded an $r^2$ of .0001 and a slope indistinguishable from zero. By both the Cochran and the Hartley tests for homogeneity of variance, samples were significantly more variable than the standards at less than the .05 level. Furthermore, the Kurtosis indices for the standards were only −0.8 and −0.6, whereas the Kurtosis index for the samples was +0.7. Thus, the variability in umbilical cord blood lead concentrations markedly exceeded the analytical variability.

Independent of the internal checks of reliability, we analyzed a series of samples that were supplied by other laboratories. In the quarterly blind comparisons sponsored by the Centers for Disease Control (Blood Lead Reference Program), the average of the absolute value of the difference between our values and theirs was 1.4 μg $dl^{-1}$ for five


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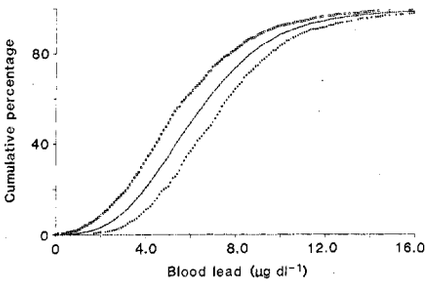


Fig. 1. The cumulative percentage of occurrences of umbilical cord blood lead concentrations. The middle curve is for all samples collected over 2 years; the other two curves are composites of data for the 3 months with the highest and the lowest average blood lead concentrations. It may be seen that the shifts in average lead concentrations reflect population-wide changes rather than changes in the relative frequencies of higher or lower lead subpopulations.

samples ranging in lead concentrations from 6 to 30 $\mu$g dl$^{-1}$. Perhaps the test most free of methodological errors was our repeated analysis of the bovine liver standard furnished by the National Bureau of Standards, certified to contain 0.34 ± 0.01 $\mu$g of lead per gram. Our nine observations averaged 0.35 ± 0.03 $\mu$g g$^{-1}$ (mean ± standard error of the mean). Since these analyses were done over a period of 1.5 years, the maximum secular change in the laboratory results was 5.7 percent per year.

The mean lead concentration of all umbilical cord blood samples was 6.56 ± 3.19 (standard deviation) $\mu$g dl$^{-1}$, and the range was 0.0 to 37.0 $\mu$g dl$^{-1}$. A cumulative frequency distribution is shown in Fig. 1. Two extreme subgroups are also displayed: blood lead concentrations from infants born during April and May 1979 and August 1980 versus those of infants born in November 1980 and January and March 1981. These subgroups were chosen because they were the most extreme monthly averages. The shapes of the three populations are not noticeably different, because the shift in the mean value with season does not represent a change in occurrence of relatively higher or lower groups. It appears that the whole population rose and fell.

We found a downward secular trend by regressing the individual values of blood lead against the date of birth. The slope was −0.89 ± 0.06 (standard error) $\mu$g dl$^{-1}$ year$^{-1}$, significantly different from zero at $P < .001$, with an $r^2 = .026$. This is a decrease of 14 percent per year.

This downward trend was even more evident if the lead data were considered as daily averages. A linear regression of average lead concentrations against time yielded a significant trend [$r^2 = .13$, $N = 720$, $P < .0001$, slope = −0.91 $\mu$g dl$^{-1}$ year$^{-1}$ ± 0.09 (standard error)]. The residuals were shown by Fourier analysis to be nonrandom. There were significant cycles of 365-day and 84 ± 5-day periods. About 90 percent of the remaining variance was composed of terms with periods of less than 20 days. Therefore, a model was designed with linear and periodic terms of the form $L = A + B_1t + B_2 \cos [2\pi/84 (t - p_2)] + B_3 \cos [2\pi/365 (t - p_3)]$, where $L$ is the blood lead concentration and time $t$ begins at 11 April 1979. Phase angles ($p$) were varied to maximize the $r$ value when comparing the model with the daily average data.

The day-to-day fluctuations in daily average blood lead concentrations are more likely to be analytical artifacts than actual changes in blood lead concentrations. Although the time constant for blood lead changes in response to changes in the exposure to lead of women at term is unknown, the mean residence time of lead in the blood of healthy adult men is 36 days (*3*). Therefore, a 20-day running average of the daily average of the data was calculated, Fourier-analyzed, and modeled. The smoothing did not alter the existence of the linear, annual, or 84-day components, which were seen in the daily averages. Fitting this model to the smoothed data gave a much smaller unexplained variance ($r^2 = .72$), with $A = 7.36 \pm 0.20$, $B_1 = -0.77 \pm 0.03$, $B_2 = 0.16 \pm 0.02$, and $B_3 = 0.51 \pm 0.02$. The residuals of this model are only 9 percent as large as the variance in the raw data and 28 percent as large as the variance in the smoothed data.

Figure 2 shows the smoothed daily average data and the model. The general decline in the lead concentration of 10.5 ± 0.5 percent per year is superimposed on winter-summer variations of about 30 percent.

The mean value of the umbilical cord blood lead concentration is considerably lower than the 22 $\mu$g dl$^{-1}$ observed at the same hospital by Scanlon in 1970 (*4*). The demographic patterns of the hospital population, obstetrical and prenatal practices, and analytical methods that may have changed over the past decade could have influenced the average lead concentrations. Nevertheless, a comparison with the results of this study indicates that the lead concentrations dropped an average 7 percent per year during the 1970's. This is not very different from the 10 percent annual decrease we observed in our population during 1979 and 1980. An explanation for the

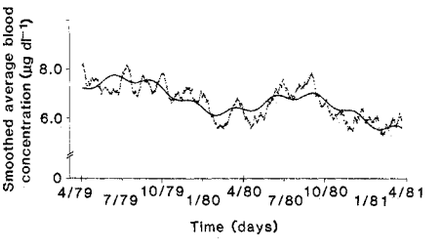


Fig. 2. A 20-day running average of umbilical cord blood lead concentrations plotted against date of birth. The ragged line is the result of smoothing the data from the daily averages of about 15 infants. It is generally higher in the summer than in the winter (7.2 versus 6.0, $P < .001$), although it has significant fluctuations. The smoother line is a model that best fits these data. It contains a declining linear term (−0.77 ± 0.03 $\mu$g dl$^{-1}$ year$^{-1}$) and two periodic terms.

decline might be decreased community-wide exposure to lead from many sources. In Boston, the drinking water supply has been modified (*5*) to decrease the lead content. Moreover, during this period, the use of alkyl lead as a gasoline additive in the United States has decreased from 278,505 short tons in 1970 to 156,000 in 1979, a drop of 5 percent per year and 17 percent per year from 1977 to 1979 (*6*). In addition to decreasing the respired lead intakes (*7*), the abatement of this dispersive use of lead could also be expected to decrease the lead in dust and in crops (*8*). Technical improvements in canning practices have also decreased the contamination of food by solder (*9*). Changes in prenatal practices, such as smoking or iron supplementation, would also affect the lead concentrations. The relative significance of these measures is not decipherable from the study, but, taken together, they could account for the observed decline. Recent evaluation by the Centers for Disease Control of the National Center for Health Statistics lead survey data (NHANES II) showed a yearly decrease of blood lead concentrations across the United States of approximately 9 percent between 1976 and 1980. This decrease could not be attributed to season, income, geography, or random variation (*10*). The most discernible environmental alteration noticed by the Centers for Disease Control was reduced lead additives in gasoline.

Possible explanations for the summer highs and winter lows might include different exposures to respirable lead, which are typically higher in summer than in winter (*1*) because of increased gasoline consumption. Of potential usefulness would be comparisons with blood data from San Diego, where the

airborne lead concentrations have a winter maximum due to a lower inversion layer (*11*).

Unlike the linear downward trend and the annual cycle, the 84-day term reflects no obvious physical cause with that frequency. Rather, its existence in both the raw and smoothed data may be an artifact of attempting to use sine waves to describe the observations, which rise more abruptly in the spring and fall more gradually in the autumn than could be described by a single sine wave.

A small number of the samples ($N$ = 323 or 2.9 percent) had lead concentrations of 1.9 $\mu g\ dl^{-1}$ or less, near the blank-dominated detection limit of our analytical system. Surveys in remote, nonurban, nonindustrial locations have yielded population means at these concentrations in adults and children (*12*). However, umbilical cord blood samples, which may be expected to exhibit lower lead concentrations, have not been measured in these investigations.

The National Health and Nutrition Survey (NHANES II) indicated that 3.9 percent of American children between 1 and 5 years of age had blood lead concentrations greater than 30 $\mu g\ dl^{-1}$, the defined threshold for undue lead exposure (*10*). The downward trend in umbilical cord blood lead concentrations over time has drastically reduced the number of infants exceeding this highest risk range. Only five of our subjects (0.05 percent) had blood lead concentrations in excess of 30 $\mu g\ dl^{-1}$. The safe limit for infants has not been established, but considerable evidence indicates that fetuses are more sensitive than children. Forward studies of neuropsychological outcome from birth onward are required to determine what level of exposure to lead is acceptable.

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## Sexual Dimorphism in the Human Corpus Callosum

Abstract. *Preliminary observations suggest a sex difference in the shape and surface area of the human corpus callosum. The sexual dimorphism is striking in the splenium, the caudal or posterior portion of the corpus callosum. The female splenium is both more bulbous and larger than the male counterpart. Since peristriate, parietal, and superior temporal fibers course through the splenium, this finding could be related to possible gender differences in the degree of lateralization for visuospatial functions.*

Although sex-related allometric variations in brain weight have been reported (*1*), to our knowledge no reliable sex differences in human brain morphology have been evidenced to date (*2*). In examining corpora callosa, we observed a sex difference in the shape of the splenium—the caudal or posterior portion of the corpus callosum. This serendipitous finding, later quantitatively substantiated, is of pragmatic interest to the forensic scientist. In addition, it has wide-ranging implications for students of human evolution and comparative neuroanatomy, as well as for neuropsychologists in search of an anatomical basis for possible gender differences in the degree of cerebral lateralization. To our knowledge, the existence of sexual dimorphism in the major cerebral commissure has not been reported and thus has promise for future research on anatomical sex differences in the human brain.

Whole normal brains [$N$ = 14: male (M) = 9, female (F) = 5] were obtained upon autopsy (*3*). All of the brains were suspended by their basilar artery in a 10 percent Formalin-saline solution (*4*) for a minimum of 3 weeks and cut midsagittally, precisely through the cerebral aqueduct. Kodachrome slides were taken of the medial aspect of the brains along with a millimeter ruler. The slides were back-projected onto a glass table, and the outline of the corpus callosum was drawn at a magnification of 1.7 to 2.2. Drawings of the corpora callosa were used for (i) gross morphological examination; (ii) computation of the anterior-to-posterior distance (callosal length) and maximum splenial width (*5*); and (iii) computer-assisted planimetric measurements of the total callosal cross-sectional surface area as well as of the partial areas of the posterior fifth, fourth, and third of the corpus callosum. The partial surface areas, which were determined on the basis of the anterior-to-posterior distance, were used as an objective quantification of splenial area since there is no natural division between the body and splenium of the corpus callosum. All of the measurements were obtained without any information on the sex, age, brain weight, and so forth, of the individual (*6*).

Gross morphological examination (Fig. 1) revealed a sexual dimorphism in the shape of the splenium. The female splenium is bulbous and widens markedly with respect to the body of the callosum. In contrast, the male counterpart is approximately cylindrical and is relatively continuous in width with the body of the corpus callosum. All drawings were correctly classified according to sex by three impartial observers on the basis of a verbal description of the sex differences.

A quantitative analysis of the maximum splenial width yielded a nearly bimodal distribution for males and females and confirmed the visual observations ($t = -5.03$; $P < .001$) (Table 1). No sex differences were found in the absolute length of the corpus callosum. However, planimetric measurements did evince a sexual dimorphism: The average area of the posterior fifth (determined to be most representative of splenial surface area) of the corpus callosum was larger in females than in males ($t = -1.85$; $P = .08$), and although the average total


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