ENVIRONMENTAL HEALTH ABSTRACTS & BIBLIOGRAPHY

FOCUS

LEAD POISONING

August 1987

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL
Atlanta, Georgia 30333

ENVIRONMENTAL HEALTH ABSTRACTS & BIBLIOGRAPHY

FOCUS

LEAD POISONING

August 1987

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL
Atlanta, Georgia 30333

Prepared by
Centers for Disease Control
Center for Environmental Health
Publications Activities
Editor: *Anne A. Olin*
Atlanta, Ga. 30333

FOREWORD

Environmental Health Abstracts and Bibliography — Focus: Lead Poisoning presents a survey of recently published literature in the field. Effort is made to keep the abstracts sufficiently informative to enable the reader to decide whether the original article would be of interest to him or her. The journals in which articles originally appeared should be checked for reprint addresses. The Centers for Disease Control (CDC) is unable to supply reprints of articles cited in this publication.

In compiling these abstracts we use the National Library of Medicine's (NLM's) interactive retrieval service, MEDLARS II. Under this system, both foreign and domestic biomedical periodicals are searched for material dealing with or related to environmental health. We also use the libraries of Emory University, CDC, and other federal agencies. Abbreviations of periodical titles are those used by MEDLARS and listed in NLM's *List of Journals Indexed in Index Medicus*.

Future issues will be devoted to various environmental health topics. Individuals wanting to be placed on the mailing key to receive future issues as published should write to the Division of Environmental Hazards and Health Effects, Center for Environmental Health, Centers for Disease Control, Atlanta, Georgia 30333.

Vernon N. Houk, M.D
Director
Center for Environmental Health

CONTENTS

GENERAL

Early Sensory-Motor Development and Prenatal Exposure to Lead

D.C. Bellinger, H.L. Needleman, A. Leviton, C. Waternaux, M.B. Rabinowitz, and M.L. Nichols. NEUROBEHAV TOXICOL TERATOL 1984 Sep-Oct;6(5):387-402.

Authors' abstract: As part of a longitudinal study of the early developmental effects of exposure to lead, we administered the Bayley Scales of Infant Development at age 6 months to infants classified into three groups on the basis of their umbilical cord blood lead levels ("low": mean = 1.8 μg/dl; "mid": mean = 6.5 μg/dl; "high": mean = 14.6 μg/dl). No infant had a cord blood lead level > 30 μg/dl, the level currently regarded as the upper limit of "normal" for young children. Multiple regression analyses indicated that high cord blood levels were associated with lower covariance-adjusted scores on the Mental Development Index. Scores on the Psychomotor Development Index were not significantly related to cord blood lead level. The level of lead in blood at 6 months of age was not associated with scores on either the Mental or Psychomotor Development Index. These data are compatible with the hypothesis that low levels of lead delivered transplacentally are toxic to infants.

The Relationship Between Prenatal Exposure to Lead and Congenital Anomalies

H.L. Needleman, M. Rabinowitz, A. Leviton, S. Linn, and S. Schoenbaum. JAMA 1984 Jun 8;251(22):2956-9.

Authors' abstract: We obtained umbilical cord blood samples from 5,183 consecutive deliveries of at least 20 weeks' gestation and analyzed them for lead concentration. Those demographic and socioeconomic variables, including lead, that were shown on univariate analysis to be associated with increased risk for congenital anomalies were evaluated and controlled by entering them into a stepwise logistic-regression model with malformation as the outcome. Coffee, alcohol, tobacco, and marijuana use, which were associated with lead level, but not risk of malformation, were also controlled. The model was reduced in steps by eliminating the variables with the highest P value, until the most parsimonious model was created. The relative risk for anomalies associated with lead was then calculated while other covariates were held constant. Lead was found to be associated, in a dose-related fashion, with an increased risk for minor anomalies.

Variability of Blood Lead Concentrations During Infancy

M. Rabinowitz, A. Leviton, and H. Needleman. ARCH ENVIRON HEALTH 1984 Mar-Apr;39(2):74-7.

Authors' abstract: As part of a study of early childhood development, more than 200 children had their blood lead concentrations (PbB) determined semiannually during the first 2 yr of life. These children were selected from 11,837 consecutive births surveyed for umbilical cord PbB at Boston Lying-In Hospital. Candidate subjects were drawn from the highest, lowest, and middle deciles of PbB. The mean PbB was 7.2 ± 5.3 (standard deviation) μg/dl at birth and did not change appreciably with age. However, the average change in an individual's PbB every 6 months was 4 μg/dl, which was severalfold in excess of the analytical reproducibility. Only 25% of the children in the highest category at birth were in the highest category at 2 yr of age. Approximately 40% of the children remained in their immediately previous PbB tertile category. A stochastic description of these patterns of change fits the data. Our results should caution investigators who might wish to rely on a single determination to categorize children with PbB.

The Neurobehavioral Consequences of Low Lead Exposure in Childhood

H.L. Needleman. NEUROBEHAV TOXICOL TERATOL 1982 Nov-Dec;4(6):729-32.

Author's abstract: Children attending nonremedial first and second grades were classified according to the concentration of lead in their shed deciduous teeth. Children in the lowest and highest 10th percentile were studied with a detailed neuropsychological battery under blind conditions. Thirty-nine nonlead covariates were controlled either by matching or in the biostatistical analysis. High-lead children tended to have significantly lower IQ scores, particularly on the verbal scales of the WISC-R, impaired auditory and language processing, and increased reaction times at longer intervals of delay. Their teachers, who were blind to the dentine lead levels, found an increased incidence of disordered classroom

behavior in direct relationship to the concentration of lead in their teeth. Quantitative electroencephalographic analysis demonstrated decreased midline α and increased midline δ in high-lead subjects. Four years later a subsample of these children was followed up and observed during quiet classroom activity. High-lead children tended to spend more time off tasks staring at classmates, out the window, or at the observer. These observations demonstrate that lead at doses below those which are associated with frank clinical symptoms produce deficits in intelligence, attention, and auditory-language function and disordered classroom behavior.

A Prospective Study of the Neurological Effects of Lead in Children

M.R. Moore, A. Goldberg, I.W. Bushnell, R. Day, and W.M. Fyfe. NEUROBEHAV TOXICOL TERATOL 1982 Nov-Dec;4(6):739-43.

Authors' abstract: In the past 3 years, our research group has investigated the relationship between lead exposure and mental and behavioral development. This has been carried out through studies in children and studies in animals. Earlier studies in children have shown that associations might be expected between environmental exposure to lead and various aspects of cognitive and behavioral development. Our study has examined, and continues to examine, a cohort of 151 children subdivided into three groups according to the level of lead exposure during early in utero development, as assessed by maternal blood lead concentration and water lead exposure in early pregnancy. Data amassed to date include measurement of psychometric function and postnatal development at the ages of 1 and 2, together with biochemical measures of lead exposure. Assessment will continue through to early scholastic performance and will include measurement of deciduous tooth lead concentration as an integrated measure of long-term exposure.

The Effects of Lead Exposure on Urban Children: The Institute of Child Health/Southampton Study

M. Smith, T. Delves, R. Lansdown, B. Clayton, and P. Graham. DEV MED CHILD NEUROL [SUPPL] 1983;47:1-54.

From authors' abstract: A study of the associations between level of tooth lead, behavior, intelligence, and a variety of other psychological skills was carried out in the child population aged 6 to 7 years in three London boroughs. Tooth lead was estimated from the chemical analysis of shed teeth donated by children. Of the eligible children, 2,663 (62.4%) donated teeth. A study of the total population was carried out to see if those who donated teeth were representative of that population. There were small but consistent and statistically significant differences — tooth-givers being of slightly higher intelligence and showing fewer behavior problems. Selected on the basis of their tooth-lead levels and social class, 403 children were studied more intensively. They were classified into six prearranged groups — high-, medium-, and low-tooth-lead levels, with each lead group divided into two social groups, manual and non-manual. The parents of these children were intensively interviewed in their homes regarding parental interest and attitudes to education, family characteristics and relationships, the early history of the child, and the child's physical environment. The intelligence of the mother was measured. The child was then studied in school by using tests of intelligence, educational attainment, and other cognitive tasks. Teachers and parents completed standardized behavior questionnaires. The results showed that intelligence and other psychological measures were strongly related to social factors, especially social grouping. Lead level was linked to a variety of factors in the home, especially the level of cleanliness, and, to a lesser extent, maternal smoking. There was no significant link between lead level and behavior, though when rated by teachers, but not by parents, there were small and reasonably consistent non-significant tendencies for high-lead children to show more difficult behavior. Before social factors were controlled for, there were significant differences between the lead groups in measures of intelligence and two other psychological tests, the children in the high-lead groups performing worse. Once a number of social factors had been taken into account, the differences between the three lead groups (high, medium, and low) became small and statistically nonsignificant, although they remained in the same direction.

Low-Level Lead Exposure in Childhood Influences Neuropsychological Performance

J. Marecek, I.M. Shapiro, A. Burke, S.H. Katz, and M.L. Hediger. ARCH ENVIRON HEALTH 1983 Nov-Dec;38(6):355-9.

Authors' abstract: Cumulative lead exposure in 193 inner-city black children was assessed by measuring lead concentrations in the primary and circumpulpal dentine of their deciduous teeth. Lead concentrations for these children were comparable with the concentrations reported in population studies of low-income children living in inner-city areas. Analysis of the children's neuropsychological test performance showed that elevated lead levels were associated with deficits in visual-motor functioning and perceptual integration, right-left orientation, and verbal abstraction; other verbal abilities and motor functioning were not affected. Possible alternative explanations for these findings were evaluated by

examining the relationships between lead and maternal intelligence, family socioeconomic status, and perinatal indicators of neurological impairment. None of these relationships was significant. It was concluded that, even at levels usually regarded as asymptomatic, lead in the environment represents a hazard to inner-city children.

Neuropsychological Effects of Lead in Children: Interactions with Social Background Variables

G. Winneke and U. Kraemer. NEUROPSYCHOBIOLOGY 1984;11(3):195-202.

Authors' abstract: After a short and selective summary of findings from psychological studies on lead-induced cognitive dysfunction in man, our own studies in lead-exposed children are briefly described in more detail. These studies, run in the cities of Duisburg and Stolberg, were based on tooth lead levels as the principal indicator of long-term cumulative lead exposure. From a comprehensive sample of neuropsychological outcome measures, only few significant findings emerged — namely, lead-related deficits of visual-motor integration and of reaction performance, but not of general intelligence. Without exception, the observed lead effects were small compared with those of social background. An interesting interaction was found between lead exposure and social background for visual-motor integration and for reaction performance: for both these measures, but not for intelligence, the degree of association between performance deficit and lead exposure was more pronounced in socially disadvantaged children than in those from a more middle-class background. This finding was tentatively discussed within a transactional model of development. The common practice of simply controlling the effects of confounding social factors by analysis of covariance or related techniques appears doubtful in this context.

Neuropsychological Studies in Children with Elevated Tooth-Lead Concentrations. II. Extended Study

G. Winneke, U. Kramer, A. Brockhaus, U. Ewers, G. Kujanek, H. Lechner, and W. Janke. INT ARCH OCCUP ENVIRON HEALTH 1983;51(3):231-52.

Authors' abstract: Results from neuropsychological tests, collected under double-blind precautions, were evaluated for 115 school-age children (mean age: 9.4 years) living in a lead smelter area (Stolberg, FRG). Tooth-lead concentrations (PbT) from shed incisor teeth as measures of longtime lead exposure were available for these children (mean = 6.16 ppm; range: 1.9-38.5 ppm), and for 83 of them blood-lead concentrations (PbB) were available as well (mean = 14.3 μg/dl; range: 6.8-33.8 μg/dl). The following functional capacities were tested: intelligence (German WISC), perceptual-motor integration (Gottinger Formreproduktionstest = GFT, Diagnosticum for Cerebralschadigung = DCS), reaction performance (Wiener Determinationsgerat), finger-wrist tapping speed, and repetitive cancellation performance (Differentieller Leistungstest). In addition, standardized behavior ratings were obtained by the examiners, the mothers, and the teachers. Multiple stepwise regression analysis (forced solution) was calculated for outcome variables and Pb tooth, including age, sex, duration of labor, and sociohereditary background as covariates. Significant ($P < 0.05$) or near-significant ($P < 0.1$) association was established between Pb tooth and GFT performance (errors), reaction performance (false reactions), and four behavioral dimensions as rated by the mothers — namely, distractibility, restlessness, lack of information, and wasting of time; the proportion of explained variance never exceeded 6%, however. No significant association was found between PbT and WISC verbal IQ after the effects of "sociohereditary background" had been eliminated, although there was still a tendency for high-level children (PbT > 10 ppm) to be inferior to low-level children (PbT ≤ 4 ppm) by 4.6 IQ points after correction for confounding. There was a near-significant, inverse relationship between finger-wrist tapping speed and Pb blood. The results are discussed within the framework of attention-deficit disorder and compared with neurobehavioral Pb effects from animal experiments, which provide suggestive evidence for a causal relationship between developmental lead exposure and certain neurobehavioral deficits.

Lead and the Relationship Between Maternal and Child Intelligence

D.C. Bellinger and H.L. Needleman. J PEDIATR 1983 Apr;102(4):523-7.

Authors' abstract: Using regression analysis, we show that the IQ's of children with elevated levels of dentine lead (> 20 parts per million) are below those expected on the basis of their mothers' IQ's. Moreover, the amount by which a child's IQ falls short of the expected value increases with increasing levels of dentine lead in what may be a nonlinear fashion. Although lead level contributed nothing to the prediction of IQ for children with low levels of dentine lead (< 10 parts per million), it rivaled maternal IQ in importance as a predictor in the group with elevated lead values. Thus, for schoolchildren with lead burdens in the highest decile of the distribution for the urban area we sampled, the usual relationship between maternal and child IQ appears to be disrupted in a manner systematically related to lead levels in dentine.

Intelligence and Lead Toxins in Rural Children

R.W. Thatcher, M.L. Lester, R. McAlaster, R. Horst, and S.W. Ignasias. J LEARN DISABIL 1983 Jun-Jul;16(6):355-9.

Authors' abstract: Hair lead content, intelligence tests, school achievement, and motor impairment assessments were obtained from 149 public school children aged 5 to 16. Hair lead concentration significantly discriminated between groups and significantly predicted IQ scores independent of group classifications. Regression analyses showed a significant negative correlation between lead and intellectual functioning, even in the normal to gifted IQ range. These results demonstrate a continuous inverse relationship between intelligence and relatively low levels of body lead in which the higher levels of cognitive function are affected before any signs of gross motor impairment are seen.

Increased Lead and Cadmium Burdens Among Mentally Retarded Children and Children with Borderline Intelligence

M. Marlowe, J. Errera, and J. Jacobs. AM J MENT DEFIC 1983 Mar;87(5):477-83.

Authors' abstract: The relationship between subtoxic metal levels and mild mental retardation and borderline intelligence was investigated. Hair metal concentrations in a group of retarded children and children with borderline intelligence and a nonretarded control group were compared. Children in the retarded/borderline group had significantly higher lead and cadmium concentrations. Sources of lead and cadmium exposure were discussed. Although an etiological relationship was not established, findings suggest the need for a continuing reexamination of lead and cadmium poisoning concentrations because levels of these metals previously thought harmless may be associated with mental retardation and impaired intelligence.

Low Lead and Cadmium Levels and Childhood Visual-Perception Development

J. Stellern, M. Marlowe, A. Cossairt, and J. Errera. PERCEPT MOT SKILLS 1983 Apr;56(2):539-44.

Authors' abstract: This study investigated possible relationships of lead and cadmium levels to childhood visual-perceptual development. Hair-metal concentrations of lead and cadmium were analyzed in 25 children who were having learning problems. They were also administered the Bender Visual-Motor Gestalt Test. Lead and cadmium levels correlated significantly and negatively with age-deviations of Bender errors. A continuing reexamination of lead and cadmium levels is needed because levels previously thought harmless may be associated with decrements in childhood visual-perceptual development.

Language and Speech Behaviors of Children with Undue Lead Absorption: A Review of the Literature

S.A. Mayfield. J SPEECH HEAR RES 1983 Sep;26(3):362-8.

Author's abstract: This article reviews the effects of chronic undue or low lead absorption on the speech and language behavior of children. Although the effects of high-level lead poisoning have been documented, the effects of chronic low-lead absorption remain controversial. It is concluded that the evidence supports the presence of speech and language problems in some low-lead level children. The severity, duration, and specific nature of the problems, however, are not clear. Pertinent research issues are addressed.

Blood Lead, Behaviour and Intelligence Test Performance in Preschool Children

P.G. Harvey, M.W. Hamlin, R. Kumar, and H.T. Delves. SCI TOTAL ENVIRON 1984 Dec;40:45-60.

Authors' abstract: A variety of measures of behavior and cognitive performance were taken on a group of preschool children together with a sample of venous blood. The relationship between blood lead and intelligence was small and statistically nonsignificant after other factors influencing cognitive performance were controlled for.

Lead and Hyperactivity Revisited. An Investigation of Nondisadvantaged Children

R. Gittelman and B. Eskenazi. ARCH GEN PSYCHIATRY 1983 Aug;40(8):827-33.

Authors' abstract: The purposes of this study were to examine whether hyperactive children had elevated lead levels, to assess whether lead levels were associated with poor psychometric performance in hyperactive children, and to replicate previous reports of hyperactive children with perinatal insult having lower lead levels than those with normal perinatal history. Hyperactive, learning-disabled children and normal siblings were studied. The hyperactive children had higher chelated urine lead levels than their own siblings. Other contrasts were not significant. Cognitive performances and lead levels were weakly associated in the hyperactive sample. Contrary to previous reports, lead levels and perinatal complications were not negatively correlated. These results support the notion that lead levels are weakly associated with hyperactive disorders.

A Pilot Study on the Metal Levels in the Hair of Hyperactive Children

P.J. Barlow. MED HYPOTHESES 1983 Jul;11(3):309-18.

Author's abstract: The concentration of a number of metals has been determined in the hair of 68 children who have been described as "hyperactive." These children are compared with a control group. The most important findings would appear to be a raised level of manganese and a reduced level of zinc in the hyperactive children. The possible significance of this is discussed. A high manganese level in learning disabled children has also recently been reported and may be of direct relevance to the present study.

Developmental Changes in Slow Cortical Potentials of Young Children with Elevated Body Lead Burden: Neurophysiological Considerations

D. Otto and L. Reiter. ANN NY ACAD SCI 1984;425:377-83.

Authors' abstract: The effects of age and blood lead level (PbB) on slow cortical potentials elicited during classical conditioning were studied in children aged 13 to 75 months. At normal PbB levels (< 30 μg/dl), slow wave (SW) voltage tended to be positive in children under 5 years old and negative in children over 5 years. A reverse age-related polarity shift was observed in children with elevated PbB levels (Otto et al., 1981). Evidence indicative of excitatory (or disinhibitory) effects of Pb exposure in immature animals (associated with hyperactivity in animals and children) was reviewed. Reversals in locomotor activity (hypoactivity) and electroconvulsive activity have also been noted in adult animals exposed to Pb as pups. Neurophysiological evidence suggests that slow surface-positive potentials in very young children may reflect axodendritic inhibitory processes. As the cortex matures, the locus of inhibitory activity shifts deeper to axosomatic connections. Negative slow potentials observed in older children, therefore, are presumed to reflect the surface-negative (dendritic depolarization), depth-positive (somatic hyperpolarization) dipole hypothesized by McSherry (1973) as the neurophysiological substrate of the contingent negative variation (CNV). Although the developmental model of the CNV proposed here is based on preliminary data and is clearly speculative, the implications of the model and data merit consideration. Positive shifts observed in very young children during the CS-UCS [conditioned stimulus-unconditioned stimulus] interval suggest why previous investigators have had great difficulty in eliciting contingent negative variation in subjects younger than 5 years. The data also suggest that body Pb burden at any level produces an observable effect on central nervous system (CNS) function. Further study is needed to replicate and clarify these findings.

Effects of Low to Moderate Lead Exposure on Slow Cortical Potentials in Young Children: Two Year Follow-Up Study

D. Otto, V. Benignus, K. Muller, C. Barton, K. Seiple, J. Prah, and S. Schroeder. NEUROBEHAV TOXICOL TERATOL 1982 Nov-Dec;4(6):733-7.

Authors' abstract: A follow-up study of slow cortical potentials in children with elevated blood lead (PbB) histories was conducted 2 years after initial evaluation. An age x PbB interaction was again observed wherein slow wave (SW) voltage varied as a linear function of PbB, with the slope of the function dependent on age. The linear relationship of SW voltage and PbB was significant by using either original PbB values (14-55 μg/dl), follow-up values (11-39 μg/dl), or the mean of the two PbB values. No evidence of a threshold for this effect was observed. The similarity of results obtained at initial and follow-up assessments suggests that the observed alterations in CNS function are persistent, despite a significant decrease in mean PbB across time. The observed change in SW voltage at PbB levels previously considered to be harmless suggests the need to reconsider the currently accepted 30 μg/dl threshold for undue lead absorption in children.

Occupational Lead Neurotoxicity: A Behavioural and Electrophysiological Evaluation. Study Design and Year One Results

E.L. Baker, R.G. Feldman, R.A. White, J.P. Harley, C.A. Niles, G.E. Dinse, and C.S. Berkey. BR J IND MED 1984 Aug;41(3):352-61.

Authors' abstract: To evaluate the effects of chronic lead exposure on the nervous system in adults, we administered a set of neurobehavioral and electrophysiological tests to 99 lead-exposed foundry employees and 61 unexposed workers. Current and past blood lead concentrations were used to estimate the degree of lead absorption; all previous blood lead concentrations had been ≤ 90 μg/100 ml. Characteristic signs (such as wrist extensor weakness) or symptoms (such as colic) of lead poisoning were not seen. Sensory conduction in the sural nerve was not affected. By contrast, various neurobehavioral functions deteriorated with increasing lead burden. Workers with blood lead concentrations between 40 and 60 μg/100 ml showed impaired performance on tests of verbal concept formation, visual/motor performance, memory, and mood. Thus, impairment in central nervous system function in lead-exposed adults occurred in the absence of peripheral nervous system derangement and increased in severity with increasing lead dose.

The Role of Occupational Lead Exposure in the Genesis of Psychiatric and Behavioral Disturbances

E.L. Baker, R.G. Feldman, R.F. White, and J.P. Harley. ACTA PSYCHIATR SCAND [SUPPL] 1983;(303):38-48.

Authors' abstract: In a prospective study of lead neurotoxicity, exposed foundry workers and referents were evaluated by using a comprehensive set of neurobehavioral tests. Other performance indexes were used, including a questionnaire, physical examination, and nerve conduction testing. Results show increased rates of depression, confusion, anger, fatigue, and tension among workers with blood levels over 40 μg/dl. Other aspects of neurobehavioral function, including verbal concept formation, memory, and visual/motor performance, were also impaired. In view of the large number of individuals exposed to lead in their work, specific inquiries should be made of individuals with affectual complaints to clarify the nature of their work and workplace exposure to lead.

A Prospective Follow-Up Study on Psychological Effects in Workers Exposed to Low Levels of Lead

P. Mantere, H. Hanninen, S. Hernberg, and R. Luukkonen. SCAND J WORK ENVIRON HEALTH 1984 Feb;10(1):43-50.

Authors' abstract: A prospective follow-up study on new lead workers who began work at a storage battery factory was carried out between 1975 and 1981. Psychological performances (e.g., intelligence, memory, visuomotor functions, vigilance, and personality) were assessed before the commencement of exposure and after 1, 2, and 4 years of work. Of an initial number of 89 workers, 24 were available for the 1-year, 16 for the 2-year, and 11 for the 4-year reexamination. The time-weighted average blood lead values ranged between 0.68 and 2.17 μmol/l (14 and 45 μg/100 ml, respectively). A reference group, nonexposed workers in a cable manufacturing plant and an electrical power plant, was similarly followed. Initially, the average psychological performances were similar among the lead workers and the referents. For some of the psychological tests learning effect, which was clearly evident among the referents during the follow-up, was almost absent among the lead workers. The lead workers' visual intelligence and visuomotor functions in particular were impaired significantly after the first 2 years of follow-up. When the lead workers were divided into two groups according to the median time-weighted average of the blood lead values (1.30 μmol/l), the Block Design and the Santa Ana coordination tests were those that best separated the subgroups. Although the impairment of the lead workers' performance was rather slight and the dispersion in the psychological changes was wide, it was evident that some higher nervous functions were affected by lead levels above about 1.45 μmol/l.

Subclinical Neurotoxic Lead Effects: Two-Year Follow-Up Studies with Psychological Test Methods

P. Mantere, H. Hanninen, and S. Hernberg. NEUROBEHAV TOXICOL TERATOL 1982 Nov-Dec;4(6):725-7.

Authors' abstract: Using a prospective, follow-up approach, we tested a group of storage battery plant workers by means of a number of psychodiagnostic tests, as e.g., subtests of the WAIS and WMS, the Bourdon-Wiersma test, and the Santa Ana test, before and 2 years after they entered the lead-works. Their performance was compared with that of an age-equivalent group of nonexposed controls. Blood lead (PbB) levels of the lead group increased from an initial 15.3 ± 6.7 μg/dl (Mean ± SD) to a final 30.5 ± 9.6 μg/dl after 2 years, whereas the corresponding PbB value of the controls was 10.5 ± 3.7 μg/dl and 10.3 ± 4.0 μg/dl, respectively. In the primary psychological examination there were no detectable performance differences between the exposed and the controls. Whereas the control group displayed pronounced performance improvement due to training for most of the tests over the 2-year period, a sizeable portion of the exposed group exhibited even performance deterioration. Group comparisons were tested by the non-parametric $\varkappa^2$-test and the two-sided Kolmogorov-Smirnov test. The most sensitive indicators of psychological impairment among the lead workers were the Block Design test, the Santa Ana coordination test, and the Digit Span test. It is concluded that the impairment of central nervous system (CNS) function, as evidenced by differential test performance, was caused by lead exposure. No exact threshold for impaired performances could be estimated.

Psychological Performance of Workers with Blood-Lead Concentration Below the Current Threshold Limit Value

P. Campara, F. D'Andrea, R. Micciolo, C. Savonitto, M. Tansella, and C. Zimmermann-Tansella. INT ARCH OCCUP ENVIRON HEALTH 1984;53(3):233-46.

Authors' abstract: The effects of lead exposure on psychological test performance and subjective feelings of well-being were investigated in 40 exposed workers whose PbB levels had never exceeded 60 μg/100 ml and in 20 controls matched for sex, age, and educational level. The exposed workers were divided into two groups of 20, with recent PbB levels in the range 45-60 μg/100

ml or below 35 μg/100 ml. The group of workers with the higher PbB levels showed significantly poorer performance and reported more physical symptoms than the other two groups. These differences were unrelated to sociodemographic and personality characteristics. A principal component analysis suggested that the poorer performance was mainly due to an impairment of general functioning and only to some extent to a deterioration in specific functions, such as verbal reasoning and abstraction. Higher lead concentrations were correlated with poorer performance and a higher number of physical complaints. These results indicate that in exposed workers the threshold for impaired performance lies below the blood-lead concentration of 60 μg/100 ml, which is the current threshold limit value (TLV).

Workplace Protection Factor Measurements on Powered Air-Purifying Respirators at a Secondary Lead Smelter: Results and Discussion

W.R. Myers, M.J. Peach 3d, K. Cutright, and W. Iskander. AM IND HYG ASSOC J 1984 Oct;45(10):681-8.

Authors' abstract: A study was conducted at a secondary lead smelter to evaluate the workplace performance of the 3M W-344 and Racal AH3 powered air-purifying respirators (PAPRs) equipped with helmets and high-efficiency filters. The research protocol developed for the study has been described in a companion paper. The results of the study indicate that the mean lead concentrations, measured inside the facepiece of both PAPRs, were significantly less than the Occupational Safety and Health Administration (OSHA) lead exposure limit of 50 $\mu g/m^3$. The means of the workplace protection factor measurements on both PAPRs were significantly less than the PAPR selection guide protection factor classification of 1,000. Correlation analysis of preshift quantitative fit factors and corresponding workplace protection factors indicated no linear association between these two measures of performance. This finding suggests that for PAPRs equipped with helmets and high-efficiency filters quantitative fit factors as presently determined are not indicative of the workplace protection that the respirators provide. Since the PAPR protection factor classification of 1,000 was originally based on quantitative fit factors, the lack of a demonstrated association between quantitative fit factors and workplace protection as found in this study may explain why their performance was significantly less than expected.

The "TWAp" in the Lead Standard

J.L. Hickey. AM IND HYG ASSOC J 1983 Apr;44(4):310-1.

Author's abstract: This paper analyzes current Occupational Safety and Health Administration (OSHA) practice for adjusting the permissible exposure limit (PEL) for inorganic lead to accommodate unusual work schedules. Depending on the work schedule, the PEL adjustment procedure can allow substantially higher exposure or require substantially lower exposure, as compared with the exposure permitted by the lead standard for a normal work schedule. In addition, the procedure allows compliance with the standard by manipulation of the work schedule alone, without reduction in lead exposure. The paper describes how calculating exposure on a weekly basis with the procedure outlined in the OSHA Field Operations Manual would eliminate the sevenfold range of allowed exposure.

Lead Neuropathy

T. Beritic. CRC CRIT REV TOXICOL 1984;12(2):149-213.

Author's abstract: The still unexplained nature of the neurotropic action of lead has prompted this chronological survey of the course of development of the medical attitude towards the problems of lead neuropathy all along the centuries — from ancient times up to the present. Once a conspicuous, severe, and even frequent clinical type of plumbism, peripheral lead neuropathy has received due attention in the early classics (Tanquerel des Planches, Duchenne, Aran, Remak, Romberg, Erb, etc.) and of the pioneers in industrial medicine (Legge, Aub, Teleky, Hamilton). Even the modern era, however, has not come further than to state that lead produces different neurological effects in different animal species and even in humans — different patterns of neuromuscular involvement. With the advent of electrophysiology, conflicting and inconsistent findings have also appeared, particularly in regard to overt and latent lead neuropathies. Theories regarding the mode and site of the neurotoxic action of lead are reviewed, and data that might be used as arguments both in favor and against are presented.

A Perspective of Lead Poisoning in Antiquity and the Present

D.E. Woolley. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):353-61.

Author's abstract: Seen in perspective, it is evident that lead poisoning is one of the earliest occupational diseases, described already thousands of years ago. The first major upswing in the history of anthropogenic production of lead was associated with the development of the Greco-Roman culture, and the most recent followed the Industrial Revolution. At the peak of the power of the Roman Empire, lead production was about 80,000 tons per year, lead and its compounds were used with great inventiveness in numerous ways, and lead poison-

ing was pandemic, with the severity of poisoning proportional to the power and status of the class. Intake of lead by the aristocracy may have been as much as 1 mg/day. The resultant mental incompetence and especially the rapidly declining birth rate among the ruling class are now believed to have been major factors in the decline of the Roman Empire. Epidemic outbreaks of lead poisoning have occurred repeatedly throughout history and still occur today. The estimated 3.5 million tons of lead produced annually during peak production in the 1970's included about 0.4 million tons of organoleads. Such intense production has increased global contamination with lead enormously. Even under relatively ideal conditions the daily intake of lead is so much higher than in prehistoric times that investigators must pause to ask themselves what a proper control group really is. Are investigators merely determining the effects of additional lead exposure on systems already greatly perturbed by lead? If so, how can we find out?

A Review of Public Health Regulations on Lead

B.L. Johnson and R.W. Mason. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):1-22.

Authors' abstract: A review of public health regulations pertaining to lead exposure is the subject of this paper. Although lead had been used for centuries in the fabrication of a host of products, it was not until the mid-nineteenth century that the clinical pattern of lead poisoning was described in the medical literature. With this recognition gradually came government health regulations designed to limit human exposure to lead from occupational and environmental sources. During the period 1890 to 1920, the British, in particular, developed comprehensive rules and regulations pertaining to occupational lead exposures. The development and imposition of U.S. health regulations occurred later in the twentieth century; federal regulations did not generally appear until the 1970's. At present, several U.S. government agencies have promulgated regulations intended to prevent lead poisoning from paint; limit lead in ambient air, drinking water, workplace environments, and consumer products; and reduce lead in fuels and fuel additives used in motor vehicles. These regulations are reviewed in terms of their extent of coverage. There is evidence, in some instances indirect in nature, that human exposure to lead in U.S. populations has been reduced, though comprehensive data are lacking. The Centers for Disease Control has reported that the mean blood lead level in the U.S.A. has decreased 36%, paralleling a reduction in the lead content of gasoline. For occupational lead exposure, comprehensive morbidity data do not exist, but an evaluation of the National Institute for Occupational Safety and Health (NIOSH) health hazard evaluations (HHE's) specific to lead shows a gradual reduction since 1977 in the percentage of HHE's for which airborne lead exceeded 0.20 mg/m^3, which at one time had been the federal standard for occupational lead exposure, before reduction of the U.S. standard to 0.05 mg/m^3.

Lead in Petrol and Levels of Lead in Blood: Scientific Evidence and Social Policy

P.C. Elwood and J.E. Gallacher. J EPIDEMIOL COMMUNITY HEALTH 1984 Dec;38(4):315-8.

Authors' abstract: Two aspects of the recent controversy about the health consequences of lead in petrol are considered. First, the evidence is shown to be deficient, largely because the basic epidemiological principles of representative sampling, realistic measurement, and control of confounding variables were not followed so that valid conclusions cannot be drawn from most of the published studies. Second, the role of science appeared to be compromised by confusion between science per se and social policy. Relations between the two are explored, and it is concluded that confusing them reduces the contribution that science can make to effective social policy.

Toxic Agent and Radiation Control: Meeting the 1990 Objectives for the Nation

D.P. Rall. PUBLIC HEALTH REP 1984 Nov-Dec;99(6):532-8.

Author's abstract: Toxic agent and radiation control is 1 of the 15 health priority areas addressed through the Public Health Service's Objectives for the Nation. Several gains in moving toward the 1990 goals for toxic agent and radiation control have been recorded. Research and technical assistance, combined with legislation to reduce the amount of lead in gasoline, have contributed to a decrease in the mean blood lead level of the general population. New testing procedures have been developed for evaluating both reproductive and developmental toxicities of chemicals. Educational implementation of pelvimetry referral criteria in a multiyear study involving approximately 200 U.S. hospitals has resulted in a 50% reduction in the number of pelvimetries performed. Health-related responses have been given to environmental problems, such as exposures to polychlorinated biphenyls (PCBs) in Massachusetts and Florida and exposures to dioxin in Missouri and New Jersey. Chemical records for some 1,000 compounds likely to occur in chemical dumps or in bulk transit are being either created or updated to enhance online data retrieval services. For the foreseeable future, however, improvement of knowledge of the potential health risk posed by toxic chemicals and radiation must remain one of the most important priorities. If toxic agents are to be controlled, development of surveillance systems and data bases is equally important.

Nutrition of Lead

S.J. DeMichele. COMP BIOCHEM PHYSIOL [A] 1984;78(3):401-8.

From author's abstract: At the levels to which human beings are exposed in the workplace as well as in the general environment, lead has been shown to be a toxic element in most of its chemical forms, whether it is inhaled or ingested in water or food. The four main sources of contamination of food are soil, industrial pollution, agricultural technology, and food processing. Reasonable quantities of the metal can be stored by humans in a relatively inert form in bone; lead has an affinity for bone and acts by replacing calcium. Gastrointestinal lead absorption and retention, the major pathway of lead intake, has been shown to vary widely depending on the chemical environment of the gastrointestinal lumen, age, and iron stores (nutritional status of the subject). Studies in animals have shown that certain substances bind lead and increase its solubility, thus enhancing its absorption. These dietary components consist of sodium citrate, ascorbate, amino acids, vitamin D, protein and fat, and lactose. Data suggest a three-compartmental pool for lead metabolism: (1) blood; (2) soft tissue (hair, nails, sweat, salivary, gastric, pancreatic, and biliary secretions); and (3) skeleton. Lead absorption occurs primarily in the duodenum where lead enters the epithelial mucosal cells. The total bodily amount of lead does not affect lead absorption; lead does not have a feedback mechanism that limits absorption. In the adult rat, lead absorption from the intestinal lumen appears to proceed by both active transport and passive diffusion. Bile is an important route of excretion in the gut.

Biotoxicity of Lead: Influence of Various Factors

K.R. Mahaffey. FED PROC 1983 Apr;42(6):1730-4.

Author's abstract: Environmental sources of lead are multiple, and a number of factors influence their toxicity. However, with the exception of tetramethyl and tetraethyl lead, the particular compound of lead seems to have relatively little influence on toxicity compared with the particle size of the source and the route and frequency of exposure. Susceptibility to lead toxicity is greater among immature animals and very young children because of their higher levels of lead ingestion, greater absorption from the gastrointestinal tract, higher percent lead retention in tissues, and greater reactivity of organs, particularly the central nervous system. Marginal nutritional status also increases susceptibility to lead toxicity. Dietary factors influencing toxicity of lead include total calories, calcium, iron, zinc, fat, ascorbic acid, and protein. Although vitamin D, specifically the metabolite 1,25-dihydroxycholecalciferol, increases lead absorption in vitamin D-deficient animals, clinical studies have shown that lead-burdened children have reduced rather than elevated plasma 1,25-dihydroxycholecalciferol levels. Bioavailability of lead, as shown by tissue lead concentrations, is not always an adequate predictor of lead toxicity. For example, concurrent exposure to cadmium results in higher toxicity of lead to the hematopoietic system, but lowers tissue lead levels substantially. Low dietary calcium increases the total body burden of lead but disproportionately increases the deposition of lead in nonosseous tissues.

Effect of Calcium and Phosphorus on the Gastrointestinal Absorption of ^{203}Pb in Man

K.C. Blake and M. Mann. ENVIRON RES 1983 Feb;30(1):188-94.

Authors' abstract: Calcium and phosphorus were mainly responsible for reducing the gastrointestinal absorption of lead in human subjects. The effect of calcium was greater than phosphorus, and their combined effect was more than additive. Increasing weights of calcium and phosphorus progressively reduced lead absorption. The relationship between absorption and increasing weights could be described by two negative exponentials. These effects could be explained if lead competed with calcium and phosphorus for common transport mechanisms in the gut. Milk was also found to reduce lead absorption. Adding milk to the diet of people with low dietary calcium intake could reduce the possibility of increased absorption of ingested lead.

Needs Assessment Under the Maternal and Child Health Services Block Grant: Massachusetts

B. Guyer, L. Schor, K.P. Messenger, B. Prenney, and F. Evans. AM J PUBLIC HEALTH 1984 Sep;74(9):1014-9.

Authors' abstract: The Massachusetts maternal and child health (MCH) agency has developed a needs assessment process that includes four components: a statistical measure of need based on indirect, proxy health and social indicators; clinical standards for services to be provided; an advisory process that guides decision making and involves constituency groups; and a management system for implementing funds distribution, namely, open competitive bidding in response to a Request for Proposals. In Fiscal Years 1982 and 1983, the process was applied statewide in the distribution of primary prenatal (MIC) and pediatric (C&Y) care services and lead poisoning prevention projects. Both processes resulted in clearer definitions of services to be provided under contract to the state as well as redistribution of funds to serve localities that had previously received no resources. Although the needs assessment process does not provide a direct measure of unmet need

in a complex system of private and public services, it can be used to advocate for increased MCH funding and to guide the distribution of new MCH service dollars.

The Pediatrician's Role in the Poison Control Movement and Poison Prevention

J.M. Arena. AM J DIS CHILD 1983 Sep;137(9):870-3.

Author's abstract: When Oliver Wendell Holmes wrote "To guard is better than to heal, the shield is nobler than the spear!" he must have had in mind the origin, many years later, of the poison control center movement. In 1952, the American Academy of Pediatrics (AAP), through a survey by its newly appointed Committee on Accident Prevention, found that the most common medical emergency in children was poisoning. The study brought forth many requests for up-to-date information on toxic ingredients in household products, as well as for improved therapeutic measures. This gave impetus to the development and implementation of poison control centers in the United States, an endeavor practically all-pediatric oriented. Then, the development of safety closures and packaging and the Poison Prevention Packaging Act in 1970 rapidly followed. This is a historical account of the AAP's role and the combined efforts of practicing and academic pediatricians in a mid-20th century movement that has saved countless children's lives.

Impact of the WIC Program on the Iron Status of Infants

V. Miller, S. Swaney, and A. Deinard. PEDIATRICS 1985 Jan;75(1):100-5.

Authors' abstract: The WIC Program (Special Supplemental Food Program for Women, Infants, and Children) was initiated in the early 1970's to improve the nutritional status of pregnant women, lactating women, and children from birth to 5 years of age who were at risk for nutritionally related health problems. Better hematologic status of a group of preschool-aged infants who were enrolled in the WIC Program from birth, as compared with another group of similar age and socioeconomic status from the pre-WIC Program era, suggests that participation in the WIC Program will help limit the development of iron depletion or iron deficiency anemia in young children, an important consideration in view of the deleterious hematologic and nonhematologic effects that have been attributed to those conditions.

Iron Fortification: An Update

J.D. Cook and M.E. Reusser. AM J CLIN NUTR 1983 Oct;38(4):648-59.

Authors' abstract: Iron fortification is the optimal approach to reducing the high prevalence of iron deficiency in developing countries. Selection of the iron source entails a compromise between the use of inert compounds, which are poorly absorbed, and chemically reactive forms with high bioavailability. Although the vehicle and fortification compound must be chosen in tandem because most iron compounds cause discoloration or rancidity, the emphasis in this review is on the food vehicle. Technology for fortifying wheat flour and bread is well established, and the use of these vehicles has probably had a significant impact on iron status in Western countries. Recent studies in India indicate that the fortification of common salt is technically feasible, and field trials have shown a good hematological response. Similar success has been achieved by fortifying refined sugar with NaFeEDTA in Guatemala. Rice has advantages as a vehicle in those areas where it is the staple food, but the technology requires further development. Fish-based condiments have been successfully fortified with NaFeEDTA and show promise as a vehicle in East Asian countries. The fortification of infant foods poses no technical problems and should be encouraged. Additional work is needed to identify other fortification options and to develop targeted fortification programs that will direct iron to those segments of a population in greatest need.

SELECTED BIBLIOGRAPHY

Anonymous. European Communities. Health and safety at work: protection of workers exposed to lead. AM IND HYG ASSOC J 1983 May;44(5):821-2.

Anonymous. Lead vs. intelligence [letter]. J PEDIATR 1983 Nov;103(5):830-2.

*Arena JM. The pediatrician's role in the poison control movement and poison prevention. AM J DIS CHILD 1983 Sep;137(9):870-3.

Atherley G. Human rights versus occupational medicine. INT J HEALTH SERV 1983;13(2):265-75.

*Baker EL, Feldman RG, White RF, Harley JP. The role of occupational lead exposure in the genesis of psychiatric and behavioral disturbances. ACTA PSYCHIATR SCAND [SUPPL] 1983;(303):38-48.

*Baker EL, Feldman RG, White RA, Harley JP, Niles CA, Dinse GE, Berkey CS. Occupational lead neurotoxicity: a behavioural and electrophysiological evaluation. Study design and year one results. BR J IND MED 1984 Aug;41(3):352-61.

*Barlow PJ. A pilot study on the metal levels in the hair of hyperactive children. MED HYPOTHESES 1983 Jul;11(3):309-18.

*Bellinger DC, Needleman HL. Lead and the relationship between maternal and child intelligence. J PEDIATR 1983 Apr;102(4):523-7.

*Bellinger DC, Needleman HL, Leviton A, Waternaux C, Rabinowitz MB, Nichols ML. Early sensory-motor development and prenatal exposure to lead. NEUROBEHAV TOXICOL TERATOL 1984 Sep-Oct;6(5):387-402.

*Beritic T. Lead neuropathy. CRC CRIT REV TOXICOL 1984;12(2):149-213.

*Blake KC, Mann M. Effect of calcium and phosphorus on the gastrointestinal absorption of ^{203}Pb in man. ENVIRON RES 1983 Feb;30(1):188-94.

*Campara P, D'Andrea F, Micciolo R, Savonitto C, Tansella M, Zimmermann-Tansella C. Psychological performance of workers with blood-lead concentration below the current threshold limit value. INT ARCH OCCUP ENVIRON HEALTH 1984;53(3):233-46.

*Cook JD, Reusser ME. Iron fortification: an update. AM J CLIN NUTR 1983 Oct;38(4):648-59.

Curran AS. Lead poisoning: a historical overview. NY STATE J MED 1984 Sep;84(9):437-8.

*DeMichele SJ. Nutrition of lead. COMP BIOCHEM PHYSIOL [A] 1984;78(3):401-8.

*Elwood PC, Gallacher JE. Lead in petrol and levels of lead in blood: scientific evidence and social policy. J EPIDEMIOL COMMUNITY HEALTH 1984 Dec;38(4):315-8.

Forbes AL, Stephenson MG. National Nutrition Monitoring System: implications for public health policy at FDA. J AM DIET ASSOC 1984 Oct;84(10):1189-93.

*Gittelman R, Eskenazi B. Lead and hyperactivity revisited. An investigation of nondisadvantaged children. ARCH GEN PSYCHIATRY 1983 Aug;40(8):827-33.

Goldberg A. A retrospect on 25 years of lead research. HEALTH BULL (Edinb) 1983 Sep;41(5):270-4.

Green DW. The saturnine curse: a history of lead poisoning. SOUTH MED J 1985 Jan;78(1):48-51.

*Guyer B, Schor L, Messenger KP, Prenney B, Evans F. Needs assessment under the Maternal and Child Health Services Block Grant: Massachusetts. AM J PUBLIC HEALTH 1984 Sep;74(9):1014-9.

Harvey PG. Lead and children's health — recent research and future questions. J CHILD PSYCHOL PSYCHIATRY 1984 Oct;25(4):517-22.

*Harvey PG, Hamlin MW, Kumar R, Delves HT. Blood lead, behaviour and intelligence test performance in preschool children. SCI TOTAL ENVIRON 1984 Dec;40:45-60.

*Hickey JL. The "TWAp" in the lead standard. AM IND HYG ASSOC J 1983 Apr;44(4):310-1.

*Johnson BL, Mason RW. A review of public health regulations on lead. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):1-22.

Lewis R. Effectiveness of employee training and motivation programs in reducing exposure to inorganic lead and lead alkyls [letter]. AM IND HYG ASSOC J 1983 Apr;44(4):B9-10.

*Mahaffey KR. Biotoxicity of lead: influence of various factors. FED PROC 1983 Apr;42(6):1730-4.

Mahaffey KR. Toxicity of lead, cadmium, and mercury: considerations for total parenteral nutritional support. BULL NY ACAD MED 1984 Mar;60(2):196-209.

*Mantere P, Hanninen H, Hernberg S. Subclinical neurotoxic lead effects: two-year follow-up studies with psychological test methods. NEUROBEHAV TOXICOL TERATOL 1982 Nov-Dec;4(6):725-7.

*Mantere P, Hanninen H, Hernberg S, Luukkonen R. A prospective follow-up study on psychological effects in workers exposed to low levels of lead. SCAND J WORK ENVIRON HEALTH 1984 Feb;10(1):43-50.

*Marecek J, Shapiro IM, Burke A, Katz SH, Hediger ML. Low-level lead exposure in childhood influences neuropsychological performance. ARCH ENVIRON HEALTH 1983 Nov-Dec;38(6):355-9.

*Abstracted

*Marlowe M, Errera J, Jacobs J. Increased lead and cadmium burdens among mentally retarded children and children with borderline intelligence. AM J MENT DEFIC 1983 Mar;87(5):477-83.

*Mayfield SA. Language and speech behaviors of children with undue lead absorption: a review of the literature. J SPEECH HEAR RES 1983 Sep;26(3):362-8.

McMichael AJ. Commentary: environmental lead and health — the tensions between social policy and scientific research. COMMUNITY HEALTH STUD 1983 Oct;7(3):314-9.

*Miller V, Swaney S, Deinard A. Impact of the WIC program on the iron status of infants. PEDIATRICS 1985 Jan;75(1):100-5.

Molina G, Zuniga MA, Cardenas A, Medina Alvarez R, Solis-Camara P Jr, Solis-Camara P. Psychological alterations in children exposed to a lead-rich home environment. BULL PAN AM HEALTH ORGAN 1983;17(2):186-92.

*Moore MR, Goldberg A, Bushnell IW, Day R, Fyfe WM. A prospective study of the neurological effects of lead in children. NEUROBEHAV TOXICOL TERATOL 1982 Nov-Dec;4(6):739-43.

*Myers WR, Peach MJ 3d, Cutright K, Iskander W. Workplace protection factor measurements on powered air-purifying respirators at a secondary lead smelter: results and discussion. AM IND HYG ASSOC J 1984 Oct;45(10):681-8.

Needleman HL. Lead at low dose and the behavior of children. NEUROTOXICOLOGY (Park Forest Il) 1983 Fall;4(3):121-33.

*Needleman HL. The neurobehavioral consequences of low lead exposure in childhood. NEUROBEHAV TOXICOL TERATOL 1982 Nov-Dec;4(6):729-32.

Needleman HL, Geiger SK, Frank R. Lead and IQ scores: a reanalysis [letter]. SCIENCE 1985 Feb 15;227(4688):701-2, 704.

*Needleman HL, Rabinowitz M, Leviton A, Linn S, Schoenbaum S. The relationship between prenatal exposure to lead and congenital anomalies. JAMA 1984 Jun 8;251(22):2956-9.

*Otto D, Benignus V, Muller K, Barton C, Seiple K, Prah J, Schroeder S. Effects of low to moderate lead exposure on slow cortical potentials in young children: two year follow-up study. NEUROBEHAV TOXICOL TERATOL 1982 Nov-Dec;4(6):733-7.

*Otto D, Reiter L. Developmental changes in slow cortical potentials of young children with elevated body lead burden. Neurophysiological considerations. ANN NY ACAD SCI 1984;425:377-83.

Palti H, Pevsner B, Adler B. Does anemia in infancy affect achievement on developmental and intelligence tests? HUM BIOL 1983 Feb;55(1):183-94.

*Rabinowitz M, Leviton A, Needleman H. Variability of blood lead concentrations during infancy. ARCH ENVIRON HEALTH 1984 Mar-Apr;39(2):74-7.

*Rall DP. Toxic agent and radiation control: meeting the 1990 objectives for the nation. PUBLIC HEALTH REP 1984 Nov-Dec;99(6):532-8.

Rimland B, Lawson GE. Hair mineral analysis and behavior: an analysis of 51 studies. J LEARN DISABIL 1983 May;16(5):279-85.

Rosner D, Markowitz G. A 'gift of God'?: the public health controversy over leaded gasoline during the 1920s. AM J PUBLIC HEALTH 1985 Apr;75(4):344-52.

Sandstead HH. Trace metals in human nutrition. CURR CONCEPTS NUTR 1984;13:37-46.

Sauberlich HE. Implications of nutritional status on human biochemistry, physiology, and health. CLIN BIOCHEM 1984 Apr;17(2):132-42.

Selvaraj MK. How to mobilize a rural community for a health programme. HYGIE 1984 Sep;3(3):9-12.

Smith M. Recent work on low level lead exposure and its impact on behavior, intelligence, and learning: a review. J AM ACAD CHILD PSYCHIATRY 1985 Jan;24(1):24-32.

*Smith M, Delves T, Lansdown R, Clayton B, Graham P. The effects of lead exposure on urban children: the Institute of Child Health/Southampton Study. DEV MED CHILD NEUROL [SUPPL] 1983;47:1-54.

Somers E. Risk estimation for environmental chemicals as a basis for decision making. REGUL TOXICOL PHARMACOL 1984 Jun;4(2):99-106.

*Stellern J, Marlowe M, Cossairt A, Errera J. Low lead and cadmium levels and childhood visual-perception development. PERCEPT MOT SKILLS 1983 Apr;56(2):539-44.

*Thatcher RW, Lester ML, McAlaster R, Horst R, Ignasias SW. Intelligence and lead toxins in rural children. J LEARN DISABIL 1983 Jun-Jul;16(6):355-9.

Valentine JM, Plough AL. Protecting the reproductive health of workers: problems in science and public policy. J HEALTH POLIT POLICY LAW 1983 Spring;8(1):144-63.

Waldron HA. Lead in bones: a cautionary tale. ECOL DIS 1982;1(2-3):191-6.

Weiss B. Behavioral toxicology and environmental health science. Opportunity and challenge for psychology. AM PSYCHOL 1983 Nov;38(11):1174-87.

*Winneke G, Kraemer U. Neuropsychological effects of lead in children: interactions with social background variables. NEUROPSYCHOBIOLOGY 1984;11(3):195-202.

*Winneke G, Kramer U, Brockhaus A, Ewers U, Kujanek G, Lechner H, Janke W. Neuropsychological studies in children with elevated tooth-lead concentrations. II. Extended study. INT ARCH OCCUP ENVIRON HEALTH 1983;51(3):231-52.

*Woolley DE. A perspective of lead poisoning in antiquity and the present. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):353-61.

*Abstracted

SOURCES AND ETIOLOGY

Sources of Lead in the Urban Environment (Editorial)

K.R. Mahaffey. AM J PUBLIC HEALTH 1983 Dec;73(12):1357-8.

From the text: A continuing controversy surrounds sources of lead to urban residents. Because lead poisoning has frequently been associated with paint, some have assumed that leaded paint is the vehicle for mild to moderate cases of lead toxicity, but others have questioned this assumption. The recent investigation of lead concentrations in inner-city garden soils sheds new light on the childhood lead exposure problem. The particular significance of this research is its demonstration for an entire major urban area that garden soils are consistently and heavily contaminated with lead. The urban clustering of high-lead soils cannot be explained simply as lead from paint leaching into soils. Rather a more general urban pattern occurs that is consistent with use of leaded gasoline and traffic density. Lead from the environment is transferred to people by a variety of routes. In addition to lead ingested from foods grown in these urban gardens, soil and dust are also ingested by children during normal developmental processes (mouthing of hands, toys, and other objects; creeping, etc.). As environmental lead pollution is brought under control, human lead exposure likewise decreases. For example, following reduction in lead sources during the 1970's a 37% decline in blood lead levels was observed between 1976 and 1980. Although a number of potential factors responsible for the decrease were considered, the most probable explanation is reduced atmospheric pollution from leaded gasoline. These changes reflect public health gains achieved in the 1970's. Because of the persistence of environmental lead, population screening for pediatric lead exposure, especially in urban areas, must be continued and measures to control atmospheric lead pollution must not be relaxed.

The Continuing Hazard of Lead Exposure and Its Effects in Children

J.J. Chisolm Jr. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):23-42.

Author's abstract: Recent epidemiological data in U.S. children aged 6 months to 5 years have shown that an estimated 4%, or approximately 675,000 children, have increased lead absorption (i.e., blood lead concentration (PbB) $\geq$ 30 μg Pb/dl (μg%) whole blood). The rate was highest among low income, inner city black children, among whom 18.6, or approximately 159,000 show PbB $\geq$ 30 μg%. There have been substantial reductions in the use of lead in gasoline and in lead in food during the past 4 years. Although the use of lead in residential paints was banned in the U.S.A. in 1977, a large stock of lead-painted old housing remains in use today. Until this substandard old housing is completely renovated or replaced, it will remain the principal environmental lead hazard for young children. Regarding effects of lead in the central nervous system (CNS), there is agreement on the following: 1) sustained PbB $\geq$ 60 μg% during the early preschool years substantially increases the risk of later learning impairment in school, 2) sustained PbB $\geq$ 40 μg% may increase the risk significantly but moderately, 3) the clinical significance of sustained PbB during early childhood in the range of 25-40 μg% remains uncertain, and 4) prospective longitudinal studies are essential to delineate the CNS effects of low level lead exposure. The primary screening test for increased lead absorption is the free erythrocyte protoporphyrin (FEP) micro test. This test will detect 95% or more of children with PbB $\geq$ 50 μg%; however, less than 50% are detected by the FEP test when PbB = 30-50 μg%.

The Present Status of Biological Effects of Toxic Metals in the Environment: Lead, Cadmium, and Manganese

G.S. Shukla and R.L. Singhal. CAN J PHYSIOL PHARMACOL 1984 Aug;62(8):1015-31.

From authors' abstract: The number of reports concerning the chemical toxicology of metals that are released in the environment by natural and anthropogenic sources has been increasing constantly. Lead, cadmium, and manganese have various uses in industry, craft, and agriculture because of their physical and chemical properties. The environmental burden of heavy metals has been rising substantially by smelter emission in air and waste sewage in water. Further, organic compounds of lead and manganese used as antiknock substances in gasoline are emitted into the atmosphere by automobile exhaustion. Such environmental contamination of air, water, soil, and food is a serious threat to all living kinds. Although these metals are known to produce their toxic effects on a variety of body systems, much emphasis has been placed on their effects on the nervous system

because of the apparent association of relatively low or "subclinical" levels of metallic exposure with behavioral and psychological disorders. Clinical and animal data on environmental exposure show that although lead and manganese are most toxic to the nervous system, cadmium exerts profound adverse effects on the kidneys and the male reproductive system. It appears that the consequences of exposure to lead in adults are less severe than the types of exposure associated with hyperactivity in neonates. Except for a few reports, hyperactivity has indeed been observed in animals exposed to either of these three metals. Experimental work has also shown that these metals produce behavioral changes by altering the metabolism of brain neurotransmitters, especially catecholamines. Recently, it is hypothesized that these metals exert their toxic effect by damaging biological defenses that exist in the body to serve as protective mechanisms against exogenous toxins. A voluminous publication list with diverse opinions on the biological effects of metals is available, and there is an urgent need to compile an assessment of the existing literature to identify the future theme of research work. The problem of metal toxicity becomes even more complex because of simultaneous or successive exposure of the general population to different physical, chemical, biological, and psychological factors in the environment. The net toxic manifestations produced by multiple exposure should, therefore, be different from those produced by a single factor as the result of their additive, synergistic, or antagonistic action. Even though a metal may not exist in sufficient amounts to cause any disability, the toxicity could result when a second factor is also present.

Identification of Lead Sources in California Children Using the Stable Isotope Ratio Technique

Y. Yaffe, C.P. Flessel, J.J. Wesolowski, A. del Rosario, G.N. Guirguis, V. Matias, J.W. Gramlich, W.R. Kelly, T.E. Degarmo, and G.C. Coleman. ARCH ENVIRON HEALTH 1983 Jul-Aug;38(4):237-45.

Authors' abstract: Two case studies are presented in which the lead isotope ratio method is applied to the identification of lead sources in 12 Oakland, California, children. One study examined lead sources in 10 children, ages 3 to 15 yr, living together as an extended family in dilapidated housing close to a busy freeway. Eight children had elevated blood lead levels ($\geq$ 30 μg/dl), and six children also had elevated erythrocyte protoporphyrin levels ($\geq$ 50 μg/dl). A second case study examined 2-yr-old male twins, both with elevated blood lead and erythrocyte protoporphyrin levels, living in a modest, but well-maintained inner city duplex apartment. Paint and surface soil samples collected in and around both households had high lead concentrations. Paint concentrations ranged from 2.9 to 273 mg/g, and surface soil concentrations ranged from 0.48 to 7.1 mg/g. The isotopic ratios of lead in the blood of these children were close to the average lead ratios of paints from exterior walls and to the lead ratios of surface soils in adjacent areas where the children played. In both case studies, the data suggest that the lead in the soil was derived mainly from weathering of lead-based exterior paints and that the lead-contaminated soil was a proximate source of lead in the blood of the children.

Environmental Lead Exposure of an Urban Indian Population

R.N. Khandekar, U.C. Mishra, and K.G. Vohra. SCI TOTAL ENVIRON 1984 Dec;40:269-78.

Authors' abstract: Environmental lead exposure of the Greater Bombay population has been estimated by measuring lead concentrations in air particulates, water, food, and cigarette smoke. Atmospheric lead concentrations in different zones of the city varied between 82 and 605 ng/m^3. The dietary intake of lead is estimated to be 245 μg/day and is calculated from the lead content in different food groups and the amount of that group consumed by an average resident of the city. The uptake by a nonsmoker living in the city area is estimated to be 33 μg of lead per day, 75% of which comes from food, 15% from air, and 10% from water. For a suburban resident 85% of the lead intake comes from food. The blood lead measurements and the contribution of atmospheric lead to the blood lead level are discussed.

Omaha Childhood Blood Lead and Environmental Lead: A Linear Total Exposure Model

C.R. Angle, A. Marcus, I.H. Cheng, and M.S. McIntire. ENVIRON RES 1984 Oct;35(1):160-70.

Authors' abstract: Most experimental and population studies of blood lead (PbB) and environmental lead, including the Omaha study, have utilized the Goldsmith-Hexter log-log or power function model. Comparison was made of the log-log model and a linear model of total exposure to describe the Omaha Study of 1,074 PbBs from children aged 1-18 years as related to air (PbA), soil (PbS), and housedust (PbHD) lead. The data fit of the linear model was statistically equivalent to the power model, and the predicted curves were biologically more plausible. The linear model avoids the mathematical limitations of the power model, which predicts PbB zero at PbA zero. From the Omaha data, this model, ln PbB = ln (β_0 + B_1 PbA + B_2 PbS + β_3 PbHD) predicts that PbB increases 1.92 μg/dl as PbA increases 1.0 μg/m^3. Since PbS and PbHD increase with PbA, however, the increases in total exposure predict a PbB increase of 4-5 μg/dl as PbA increases 1.0 μg/m^3.

Lead in Umbilical Blood, Indoor Air, Tap Water, and Gasoline in Boston

M. Rabinowitz, H. Needleman, M. Burley, H. Finch, and J. Rees. ARCH ENVIRON HEALTH 1984 Jul-Aug;39(4):299-301.

Authors' abstract: A strong statistical correlation was found among the monthly averages of lead concentrations in umbilical cord blood (about 500 births/month), indoor air (12 sites/month), and gasoline lead sales between March, 1980 and April, 1981 in Boston. Tap water lead (24/month) variations did not correlate with blood lead in this population.

Human Exposure to Heavy Metals in East Greenland. II. Lead

J.C. Hansen, N. Kromann, H.C. Wulf, and K. Alboge. SCI TOTAL ENVIRON 1983 Feb;26(3):245-54.

Authors' abstract: The concentration of lead in 175 blood samples originating from the district of Angmagssalik, East Greenland, and 130 from Aarhus, Denmark, has been determined. Both Greenland and Danish males had significantly higher (5%) blood lead than females (Eskimoan males 14.8 μg Pb/100 ml, females 12.8 μg Pb/100 ml; Danish males 10.5 μg Pb/100 ml, females 7.7 μg Pb/100 ml). For Danes living temporarily in Greenland the values were the following: males 10.5 and females 10.2 μg Pb/100 ml. Eskimos of both sexes were found to have higher blood lead values than Danes living in the same area. Danish males from Greenland and Denmark were not found to be different, whereas Danish women living in Greenland had a significantly higher (5%) mean value than women living in Denmark. In the Eskimo group, but not in the Danish, a weak, positive, but significant age correlation was found. Four samples of Eskimo origin exceeded 35 μg Pb/100 ml, which is accepted in the EEC as a maximum value for nonoccupationally exposed persons. When reexamined 5 months later, all values were below this limit. The influence of eating habits (local or imported food) and smoking habits was tested, but not found to influence the blood lead concentration. The results have confirmed that blood lead levels in Greenland are comparable to those found in European industrialized areas. The reason for the unexpected high level in the arctic area with minimum car driving and industry remains to be clarified.

Direct and Indirect Chemical Exposure in Children

L.K. Garrettson. CLIN LAB MED 1984 Sep;4(3):469-73.

Author's abstract: Like adults, children are at risk from chemicals in the environment; unlike adults, the cause of their risk is due to developmental factors. Because organs such as the brain are developmentally incomplete in children, there is the potential for effects on maturation that are not seen in the adult. Environmental and occupational safety considerations need to include children because of the potential for toxins to be transported—for example, via clothing and the air we breathe.

Circumstances Surrounding Deaths from Accidental Poisoning 1974-80

A.W. Craft. ARCH DIS CHILD 1983 Jul;58(7):544-6.

Author's abstract: The deaths of 99 children under 5 years of age were studied through the coroners' records. Sixty-nine deaths were caused by medicines—most of which were prescribed for mother, were recently dispensed, and currently in use. Household products accounted for 11 deaths, lead poisoning for 6, carbon monoxide for 5, and "medical mishaps" for 8. [The six children who died from lead encephalopathy were known to have eaten old paint; one child may have been poisoned by the lead-containing eye makeup, Surma.] Prevention lies in both education and more effective and selective use of child-resistant containers.

Lead Poisoning Among Children in Saudi Arabia

M.A. Abdullah. J TROP MED HYG 1984 Apr;87(2):67-70.

Author's abstract: Six Saudi children aged between 10 and 30 months were found to have lead poisoning. Two of them presented with encephalopathy. Twenty children with unexplained convulsions, some of whom died, were reported to have been admitted to the local district hospital recently. All our cases were diagnosed within 2 weeks of the index case being diagnosed. The source of lead was found to be a locally used teething powder known as "Saoott" and "Cebagin." This was prescribed by a traditional healer. The lead content of this powder was found to be 51%. Chemical analysis of other locally used eye cosmetics and teething medicines showed a lead content of up to 88%. The difficulties faced in diagnosis and management of these cases in developing countries are discussed. The importance of prevention is stressed.

Lead Poisoning in a West Bank Arab Village

C. Hershko, A. Abrahamov, J. Moreb, M. Hersh, R. Shiffman, A. Shahin, E.D. Richter, A.M. Konijn, E. Weissenberg, F. Graver, et al. ARCH INTERN MED 1984 Oct;144(10):1969-73.

Authors' abstract: Eleven patients from the West Bank village of Es-Sawiyeh were admitted with lead poisoning to two Jerusalem hospitals between November 1982 and

Changes in Urinary δ-Aminolevulinic Acid at Low Lead Exposure Level with Special Reference to Production Activity

K. Sato, H. Fujita, S. Inui, and M. Ikeda. INT ARCH OCCUP ENVIRON HEALTH 1983;52(1):25-32.

Authors' abstract: A 7-year follow-up survey on 53 workers was carried out in a lead storage battery factory to evaluate the significance of urinary δ-aminolevulinic acid (ALA) and blood lead in a work environment where lead in the air was considered to be about or less than the current occupational exposure limit. Although lead in the blood and ALA in the urine had a good correlation to each other cross-sectionally as well as longitudinally, geometric means of lead concentrations in the workroom air samples, which were collected following grid sampling strategy, did not correlate with ALA in urine significantly. On the contrary, the semiannual production of batteries significantly correlated with changes in mean ALA in urine. The questionnaire survey proved that the prolongation in work hours leads to an increase in the mean ALA in urine as well as a higher incidence of higher-than-normal urinary ALA. The results clearly demonstrated the importance of the biological indicators, such as lead in blood and urinary ALA, as well as the necessity of paying attention to nonindustrial hygiene factors, such as the production rate of batteries and the length of the daily shift, for the protection of the workers' health when lead in the air is moderate.

Lung Cancer Mortality Among Workers Making Lead Chromate and Zinc Chromate Pigments at Three English Factories

J.M. Davies. BR J IND MED 1984 May;41(2):158-69.

Author's abstract: Lung cancer mortality among 1,152 men working at three English chromate pigment factories was studied from the 1930's or 1940's until 1981. Workers at factory C were exposed only to lead chromate and experienced normal mortality (Obs/Exp deaths 7/6.45). Workers at factories A and B were exposed to both lead and zinc chromate; mortality was normal among those who had only low exposure (O/E 7/6.95). For workers with high or medium exposure, lung cancer mortality was significantly raised among men remaining at least a year after entering service at factory A during 1932-54 (O/E 21/9.45) and at factory B during 1948-67 (O/E 11/2.50). At factory A, 1933-46 entrants staying only 3-11 months were not affected (O/E 6/5.04), and 1955-63 entrants also appeared unaffected (O/E 2/2.00); working conditions there improved in 1955. The hazard at factories A and B affected workers who left after 1 year as well as those with longer service, and latent intervals were unusually short. The results indicate that moderate or heavy exposure to zinc chromate may give rise to a severe risk of developing lung cancer, but that exposure which is relatively mild or lasts less than a year may not constitute an effective risk. The results provide no indication that lead chromate induces lung cancer in man, even under conditions conducive to lead poisoning.

Long-Term Mortality Study of Chromate Pigment Workers Who Suffered Lead Poisoning

J.M. Davies. BR J IND MED 1984 May;41(2):170-8.

Author's abstract: Long-term mortality was studied in a group of 57 chromate pigment workers who suffered clinical lead poisoning, mostly between 1930 and 1945. One death was attributed to lead poisoning, and there were significant excesses of deaths from nephritis (observed/expected 3/0.24) and cerebrovascular disease (9/2.20), as well as nonsignificant excesses for respiratory diseases (7/3.59) and accidents and violence (3/1.13). The deaths from nephritis followed long spells of service exceeding 10 years. Poisoning appeared to have more adverse long-term effects on older workers: 15 men aged 40 or over at the time of acute poisoning experienced generally high mortality, and 30 years later or by the end of 1981 only 2 survived instead of the 7 expected. The risk of cerebrovascular disease appeared to be unrelated to duration of exposure and affected even men employed for under 1 year. Excluding the 57 lead-poisoned men, other contemporary workers at the factories showed no excess mortality from cerebrovascular disease.

Increased Urinary Enzyme Excretion in Workers Exposed to Nephrotoxic Chemicals

B.R. Meyer, A. Fischbein, K. Rosenman, Y. Lerman, D.E. Drayer, and M.M. Reidenberg. AM J MED 1984 Jun;76(6):989-98.

Authors' abstract: Nephrotoxic chemicals are commonly present in the environment, particularly in the workplace. The level of occupational exposure to these chemicals has been so reduced that exposure to these agents now rarely causes clinically evident acute renal disease. A sensitive indicator of renal injury, urinary excretion of N-acetyl-β-glucosaminidase, was utilized to evaluate persons exposed in the workplace to lead, mercury, or organic solvents, for evidence of renal effects from this exposure. None of the persons had clinically evident renal disease by history, none had hypertension, and all had normal findings on urinalysis. When compared with appropriate control populations, workers exposed to lead, workers exposed to mercury, and two of three groups of workers exposed to organic solvents had significant increases in urinary acetyl glucosaminidase activity. The third group of laboratory workers with low exposure to organic solvents had no increase in urinary acetyl glucosaminidase activity. Exposure to environ-

mental nephrotoxins at levels currently considered safe can produce renal effects as manifested by elevations of urinary acetyl glucosaminidase excretion; these renal effects are not always innocuous.

Biological Monitoring of Lead Effects in a Smelter Community Before and After Emission Control

D. Prpic-Majic, J. Meczner, S. Telisman, and A. Kersanc. SCI TOTAL ENVIRON 1984 Jan 27;32(3):277-88.

Authors' abstract: Biological monitoring of lead effects in specific population groups living in the vicinity of a lead smelter has been followed up after effective emission control, in order to estimate the length of time necessary before the characteristic indicators of increased lead absorption normalize. The period established could be a realistic basis for predicting the time necessary to elapse before a lead-contaminated area can be proclaimed as safe for normal living. Three groups of subjects were examined: preschool children, school children, and mothers. The biological monitoring included the measurement of δ-aminolevulinic acid dehydratase activity (ALAD) and the concentration of zinc-protoporphyrin (ZPP), blood lead (Pb-B), and hemoglobin (Hb). The results obtained demonstrated a gradual normalization of the characteristic indicators of lead absorption, although they were still outside corresponding values in the control group even 4 years after the installation of effective emission control. These findings emphasize the advantages of biological monitoring over environmental for objective assessment of internal and external lead exposure following effective engineering control of the emission source.

Lead Pollution in Antwerpen, Belgium

W.J. Eylenbosch, M.P. van Sprundel, and R.R. Clara. ANN ACAD MED SINGAPORE 1984 Apr;13(2):224-30.

From authors' abstract: Environmental pollution by trace metals was found to be important in the vicinity of a smelter situated in Hoboken, a suburb of Antwerpen, Belgium. Lead content of surface soil ranged from 147-693 ppm, and dust samples contained up to 7% of lead. The annual average ambient air concentration decreased from 3.79 μg Pb/m^3 in 1974 to 1.25 μg Pb/m^3 in 1982. Lead deposition in fall-out samples was about 20 mg/m^2/day at 500 m from the smelter. In 1978, the mean blood lead level of 11- to 13-year-old children was 26.9 μg/100 ml within 1 km from the smelter, compared with 16.3 μg/100 ml at 2.5 km and 11.2 μg/100 ml in a rural control group. Younger children even proved to be at higher risk of lead impregnation. Out of 359 children, 3-12 years old, attending schools within 1 km of the smelter, 23 belonged to class III of the CDC risk classification and 3 to class IV. Seventeen of them showed reduced nerve conduction velocities. The mean dentine lead level of 51 exposed children was 31.94 ± 6.98 ppm compared with 9.63 ± 1.50 ppm in an urban control group. A program aimed at reducing exposure was enforced: reduction of emission and wind-blown dust from ore-piles, decontamination of houses and soils, closing down of schools near the smelter, motivation of families for moving away from the area, and screening of the children. Although an important reduction of ambient air lead levels could be realized, lead deposition did not decrease significantly.

Lead and Cadmium Concentrations in the Hair of Fishermen from the Subae River Basin, Brazil

F. Carvalho, T.M. Tavares, S.P. Souza, and P.S. Linhares. ENVIRON RES 1984 Apr;33(2):300-6.

Authors' abstract: Previous studies have shown heavy pollution by lead and cadmium in the Subae River basin, State of Bahia, Brazil, caused by a lead smelter. Concentrations of these metals were determined in scalp hair of fishermen from three riverside towns and from a reference town. Increased levels for both metals were associated with increasing proximity to the smelter. Mean concentrations of lead and cadmium were higher among fishermen with straight hair than among those with curly hair. The effects of hair washing, hair type, and color and age on metal concentrations in fishermen's hair were studied.

The Influence of Orally-Administered Vitamin C or Zinc on the Absorption of and the Biological Response to Lead

R. Lauwerys, H. Roels, J.P. Buchet, A.A. Bernard, L. Verhoeven, and J. Konings. J OCCUP MED 1983 Sep;25(9):668-78.

Authors' abstract: A single-blind study was performed on male workers from a primary lead smelter to determine whether a daily oral supplement of vitamin C (1 g vitamin C orally once a day, five times a week for 20 weeks) or zinc (60 mg zinc as zinc gluconate once a day, five times a week for 8 weeks) influences the absorption of and the biological (hematological and renal) response to lead. The vitamin C and the zinc study groups comprised 39 and 11 workers, respectively. Their blood levels of lead at the start of the experiment ranged from 28.9 to 76.4 μg/100 ml. A matched control group receiving a placebo was followed simultaneously. The results demonstrate that, in workers whose exposure to inorganic lead is moderate and who do not suffer from nutritional deficiencies, oral supplementation of vitamin C or zinc

does not influence the metabolism and biological action of lead.

Physico-Chemical Characterization of Atmospheric Trace Metal Emissions from a Primary Zinc-Lead Smelter

R.M. Harrison and C.R. Williams. SCI TOTAL ENVIRON 1983 Nov;31(2):129-40.

Authors' abstract: Emissions from the stacks of a major primary zinc-lead smelter were characterized by using X-ray powder diffraction spectrometry (XRD). The following chemical phases were identified: $PbSO_4$, PbO X $PbSO_4$, PbO, PbS, PbO, ZnO, α-ZnS, and CdO. A complementary environmental investigation revealed that, within the works boundary, the airborne metals might be associated mainly with the fugitive blowage of coarse particles containing primary ore minerals. However, such fugitive emissions were found to be of low significance in the local environment outside the works perimeter, where fine particle emissions from the stacks of the smelter were the predominant source of airborne cadmium, lead, and zinc.

SCE Analysis in Children Exposed to Lead Emission from a Smelting Plant

L. Dalpra, M.G. Tibiletti, G. Nocera, P. Giulotto, L. Auriti, V. Carnelli, and G. Simoni. MUTAT RES 1983 Jun;120(4):249-56.

Authors' abstract: The frequency and location of sister chromatid exchanges (SCE) were evaluated in lymphocytes from peripheral blood cultures of 19 children living in a widely contaminated area and showing an increased absorption of lead. In the comparison between the exposed children and a control group living in an uncontaminated area, no significant differences were found in the mean values of SCE frequencies. The distributions of the SCE between chromosomes were proportional to chromosome length in both groups.

Sister Chromatid Exchange in Response to Variations in Occupational Lead Exposure

P. Grandjean, H.C. Wulf, and E. Niebuhr. ENVIRON RES 1983 Oct;32(1):199-204.

Authors' abstract: Sister chromatid exchange (SCE) rates in 10 long-term lead-exposed men increased significantly with increasing zinc protoporphyrin concentration in blood. SCE rates were also related to blood lead levels, but this correlation was not statistically significant. These results were obtained before the summer vacation. Six men were examined again shortly after the vacation; both SCE rates and lead-exposure parameters had decreased significantly. An increase was seen in one worker; however, this result could be related to a serious disease for which he was undergoing treatment. Continued examinations showed a tendency of increasing SCE rates and exposure parameters, but the followup was too incomplete to allow a statistical analysis. Further studies of 18 newly employed workers failed to show any increase in SCE during the first 4 months of employment despite some increases in both zinc protoporphyrin and lead levels in the blood. The results obtained suggest that a genotoxic effect due to inorganic lead may occur in long-term lead-exposed workers.

Combined Effects of Lead and EDTA on Na^+,K^+-ATPase Activity of Erythrocyte Membranes

I. Karai, S.I. Lee, S. Horiguchi, K. Fukumoto, S. Matsumura, and S. Takise. J TOXICOL ENVIRON HEALTH 1983 Oct-Dec;12(4-6):721-30.

Authors' abstract: Erythrocyte Na^+,K^+-ATPase activity increased significantly in lead workers of a lead refining factory when measured with EDTA and compared with the controls without EDTA. The enzyme activity measured with EDTA increased in the following order: controls less than office workers in a lead refining factory less than lead workers. A positive correlation existed between blood lead and enzyme activity with EDTA ($r = 0.380$, $p < 0.10$), and the activity without EDTA ($r = 0.398$, $p < 0.05$). A negative correlation was found between sodium in erythrocytes and enzyme activity with EDTA ($r = -0.437$, $p < 0.05$), and the activity without EDTA ($r = -0.416$). But no relationship was observed between enzyme activities and potassium in erythrocytes. A positive correlation between enzyme activity with EDTA and that without EDTA was observed ($r = 0.452$, $p < 0.05$). With addition of lead to fragments of erythrocyte membranes, a significant decrease occurred in the activity of the enzyme without EDTA, whereas no change was observed with EDTA. No significant change occurred in the enzyme activity with and without EDTA upon addition of lead to blood. The maximum level of lead in membrane fragments (lead combined with membranes) of workers exposed to lead was 0.60 μg/mg protein, and that in the experiment of addition to blood was 7.0 μg/mg protein.

Saccadic Eye Movements Among Copper Smelter Workers

L. Glickman, J.A. Valciukas, R. Lilis, and I. Weisman. AM J IND MED 1985;7(2):141-53.

Authors' abstract: Saccade accuracy was studied in 87 copper smelter workers. Findings were compared with those obtained in 52 lead-exposed automobile production

workers and 52 controls examined as part of a separate study. Both groups of workers showed a decrease in saccade accuracy compared with controls. Saccade accuracy was reduced in copper smelter workers over 50 years of age compared with automobile production workers in this age group. Decreased saccade accuracy was not correlated with blood lead (Pb-B), zinc protoporphyrin (ZPP), or urinary arsenic (As-U) levels among copper smelter workers, but was significantly correlated with both Pb-B and ZPP in the group of automobile production workers. Saccade accuracy decreased significantly with age and duration of exposure only in the group of copper smelter workers. Complex exposures to lead and other toxic agents present in the smelter may account for the reduction in saccade accuracy among copper smelter workers.

Occupational Lead Exposure. Effects on Saccadic Eye Movements

L. Glickman, J.A. Valciukas, R. Lilis, and I. Weisman. INT ARCH OCCUP ENVIRON HEALTH 1984;54(2):115-25.

Authors' abstract: Quantitative measures of saccadic eye movements were examined in 52 lead-exposed autobody shop workers and 52 age-matched controls with no history of occupational lead exposure. Three characteristics of saccadic eye movements were studied: 1) saccade accuracy, 2) number of overshoots, and 3) maximum velocity. The results indicated that workers exposed to inorganic lead showed a decrease in saccade accuracy and an increase in overshoots compared with controls. Saccade maximum velocity was lower in lead-exposed workers than in controls, but the difference was just short of statistical significance. Correlations between measures of saccadic eye movements and indicators of lead absorption—blood lead (Pb-B) and zinc protoporphyrin (ZPP) levels—were analyzed in the lead-exposed workers. Saccade accuracy was negatively correlated with both Pb-B and ZPP levels. The number of overshoots was not correlated with either Pb-B or ZPP levels. Saccade maximum velocity was not correlated with Pb-B, however, there was a significant negative correlation with ZPP. Age effects observed in the control group were disrupted in lead-exposed workers. In addition, saccadic eye movements in younger workers (below 30 years old) were more affected by exposure to inorganic lead than were saccadic eye movements in older workers (50 years and older). It is proposed that these findings are consistent with a relatively rapid buildup of metabolically active lead burden observed in the study group. The data suggest that quantitative assessment of eye movements may be an important tool for studying subclinical central nervous system (CNS) dysfunction due to inorganic lead exposure.

Distribution of Blood Lead, Blood Cadmium, Urinary Cadmium, and Urinary Arsenic Levels in Employees of a Copper Smelter

R. Lilis, J.A. Valciukas, J.P. Weber, A. Fischbein, W.J. Nicholson, C. Campbell, J. Malkin, and I.J. Selikoff. ENVIRON RES 1984 Feb;33(1):76-95.

Authors' abstract: A cross-sectional medical examination of a copper smelter work force included determination of blood lead (Pb-B), zinc protoporphyrin (ZPP), blood cadmium (Cd-B), urinary cadmium (Cd-U), and urinary arsenic (As-U), since it was known that such metal impurities were present in the copper concentrate. A total of 776 copper smelter employees (680 active and 96 retirees and ex-employees) were examined. Another 144 men, never employed in the smelter but who had worked in copper mines (and sometimes in gold mines), were also examined. Mean Pb-B, ZPP, Cd-B, and As-U were significantly higher in active copper smelter employees than in retirees or miners, indicating exposure and absorption in the copper smelter. Significant correlations between Pb-B and Cd-B and between Cd-U and As-U were present, confirming the common source of absorption. Although there was evidence for an increased lead absorption, this was very moderate, with practically no Pb-B levels in excess of 60 μg/dl. A marked effect of smoking on blood cadmium levels was present; nevertheless, for all smoking categories Cd-B levels were significantly higher in active employees, indicating the independent contribution of exposure to cadmium in the smelter. Cd-U did not exceed 10 μg/g creatinine, the generally accepted "critical" level for the kidney, but was higher than 2 μg/g creatinine, a level very rarely exceeded in the general population, in a sizable proportion of those examined. The highest Cd-U levels were found in retired copper smelter employees; age might have been a contributing factor, besides a longer duration of exposure in the smelter.

Relation Between Pica and Blood Lead in Areas of Differing Lead Exposure

J.E. Gallacher, P.C. Elwood, K.M. Phillips, B.E. Davies, and D.T. Jones. ARCH DIS CHILD 1984 Jan;59(1):40-4.

Authors' abstract: Surveys were conducted in four areas in Wales with differing degrees of environmental lead. In two areas the source of the lead was traffic, and in one it was spoil from lead mining in the past. The fourth area, which served as a control, was a village remote from heavy traffic, industry, and lead mining. Various environmental samples were taken, and children aged 1-3 years and their mothers were studied. Blood lead concentrations were raised in the lead mining area, and within the areas defined by traffic flow the blood lead concentrations of the mothers showed a gradient. Pica in

the children, assessed by a questionnaire, showed no relation with blood lead, but the amount of lead removed from the children's hands with "wet wipes" was an important contributor to blood lead concentrations.

Contamination of Environment with Heavy Metals Emitted from Automotives

A. Falahi-Ardakani. ECOTOXICOL ENVIRON SAFETY 1984 Apr;8(2):152-61.

Author's abstract: Interest has arisen in heavy-metal contamination of the environment, mostly because of potential hazards to the health of animals and humans (directly and/or indirectly). High levels of heavy metals in soil, plants, and the atmosphere are often related to industries, highways, chemical dumping, impure chemical fertilizers, and pesticides containing metals. An important source of heavy metals, especially lead, is from the combustion of leaded gasoline used for transportation. Other heavy metals associated with transportation include nickel, which is also added to gasoline and is contained in engine parts, zinc, and cadmium from tires, lubricating oils, and galvanized parts such as fuel tanks.

The Health Effects of Automobile Exhaust. VI. Relationship of Respiratory Symptoms and Pulmonary Function in Tunnel and Turnpike Workers

D.J. Tollerud, S.T. Weiss, E. Elting, F.E. Speizer, and B. Ferris. ARCH ENVIRON HEALTH 1983 Nov-Dec;38(6):334-40.

Authors' abstract: To examine the effect of automobile exhaust on respiratory symptoms and pulmonary function, the authors studied 175 tunnel and turnpike workers employed by the Massachusetts Turnpike Authority on two occasions 3 yr apart beginning in 1972. A standard respiratory symptom and illness questionnaire was administered, spirometry was performed, and proximal hair lead and blood lead content were measured as biologic indices of automobile exhaust exposure. One hundred and nine (63%) workers were current cigarette smokers, 41 (23%) were exsmokers, and 24 (14%) had never smoked. Smoking was strongly related to respiratory symptoms of cough ($P < .001$) and phlegm production ($P < .001$), but not to wheezing ($P = .41$), breathlessness ($P = .14$), bronchial asthma ($P = .13$), or frequent chest colds ($P = .14$). When workers were stratified by smoking status, no effect could be seen between high automobile exhaust exposure as measured by a variety of parameters and all of the above respiratory symptoms and illnesses. The level of pulmonary function [forced expiratory volume in 1 sec ($FEV_{1.0}$) and forced vital capacity (FVC)] was not related to past or current exhaust exposure in a cross-sectional analysis when we controlled for age, height, and cigarette consumption. In a prospective analysis of 84 of these workers, the observed changes in $FEV_{1.0}$ and FVC over 3 yr were unrelated to exhaust exposure after controlling for age, height, cigarette consumption, and initial level of pulmonary function.

Occupational Exposure to Lead in Ancient Times

J.O. Nriagu. SCI TOTAL ENVIRON 1983 Nov;31(2):105-16.

Author's abstract: The uses and regional production of lead in ancient times are summarized. Since there is no evidence to suggest that any deliberate attempts were made to curtail personal exposure to the mine dusts or the emissions from the forges and crucibles, it is surmised that many of the ancient artisans who worked with lead probably contracted plumbism. The number of workers so exposed is estimated to be over 140,000 per year during the Roman Empire. The ancient literary records of work-related plumbism, however, are surprisingly sparse.

In Vivo X-Ray Fluorescence Estimation of Bone Lead Concentrations in Queensland Adults

J. Price, H. Baddeley, J.A. Kenardy, B.J. Thomas, and B.W. Thomas. BR J RADIOL 1984 Jan;57(673):29-33.

Authors' abstract: A group of 200 Queensland adults without known health problems had in-vivo estimation of finger bone lead concentrations with X-ray fluorescence analysis (XRF). Forty of these subjects had elevated levels of bone lead of 25 ppm or more, consistent with exposure to the metal. Although the correlation between Queensland residence during childhood and raised bone lead levels was not significant, there were significant correlations between childhood residence in a painted wooded house and raised levels, and between occupational exposure and raised levels. Of the 40 subjects with elevated lead levels, only 2 had neither a history of occupational exposure or childhood residence in a wooden house, whereas 11 of the 25 who had a history of both occupational and residential exposure were positive. The data are consistent with lead in housepaint or absorbed during occupational exposure being the two major sources of raised bone lead concentrations.

Influence of Removal from Occupational Lead Exposure on Blood and Saliva Lead Concentrations

J. Brodeur, Y. Lacasse, and D. Talbot. TOXICOL LETT 1983 Oct-Nov;19(1-2):195-9.

Authors' abstract: Samples of total blood and unstimulated mixed saliva were obtained from five male workers

occupationally exposed to lead at various time intervals after removal from their work environment. Initial blood lead concentrations were elevated in all workers and then slowly decreased upon removal. Lead concentrations in saliva fell much more abruptly than those in blood, the saliva half-lives being estimated at 5-7 days. Temporary return to work of two workers resulted in relatively marked increases of salivary lead concentrations. These results suggest that salivary lead is closely related to recent lead exposure.

Psychological and Physical Complaints of Subjects with Low Exposure to Lead

C. Zimmermann-Tansella, P. Campara, F. D'Andrea, C. Savonitto, and M. Tansella. HUM TOXICOL 1983 Oct;2(4):615-23.

Authors' abstract: The relationship between lead uptake level and subjective psychological and physical symptoms was investigated in two groups of occupationally exposed workers with blood lead (PbB) levels between 45 and 60 μg/100 ml and below 35 μg/100 ml, respectively. Findings were compared with those of a nonexposed control group. Psychological symptomatology as defined by the GHQ [general health questionnaire] proved unsensitive to low levels of lead exposure, whereas physical symptomatology as defined by the SSQ [subjective symptoms questionnaire], in particular neurological symptoms, showed a significant tendency towards an uptake response relationship. The minimum uptake level for neurological symptoms in this study was below 35 μg/100 ml.

Evaluation of the Current Risk of Lead Poisoning in the Ceramics Industry

E. De Rosa, D. Toffolo, M. Sigon, F. Brighenti, G.P. Gori, and G.B. Bartolucci. SCAND J WORK ENVIRON HEALTH 1983 Dec;9(6):463-9.

Authors' abstract: The authors evaluate the current possibility of lead poisoning in the production of ceramic tiles, an industrial sector that has always been considered dangerous because of the use of lead-rich glazes. The study was conducted in nine plants, four of which were repeatedly monitored (five checks on 94 exposed subjects). The other five plants (for a total of 221 exposed subjects) were only checked once. An analysis of all the results showed a clear reduction in mean blood lead levels, which the authors believe was due to the use of glazes with less lead. The results obtained were generally satisfactory; they indicated a definite improvement in the situation with respect to the authors' previous investigations, even for jobs in which workers were more frequently exposed. The data overlap those observed in the production of artistic pottery, which has always been considered less dangerous.

Lead Concentrations in the Blood of Children from Pottery-Making Families Exposed to Lead Salts in a Mexican Village

G. Molina-Ballesteros, M.A. Zuniga-Charles, A. Cardenas Ortega, P. Solis-Camara R., and P. Solis-Camara V. BULL PAN AM HEALTH ORGAN 1983;17(1):35-41.

Authors' summary: Pottery-making is a common Mexican handicraft, and thousands of home workshops devoted to this trade are scattered through central and southern Mexico. This entails a risk of chronic lead poisoning through exposure to lead oxide in glazing material, a matter of particular concern because chronic lead poisoning is Mexico's third most common occupational disease. To investigate such exposure and follow up on earlier studies, we conducted a survey of the children 5 to 15 years of age in a town called Tonala in Jalisco State. A total of 153 children belonging to pottery-making families with home workshops were examined, as were 80 children from non-pottery-making families who served as a control group. Blood and urine specimens from these children showed that many of those from the pottery-making families had unusually high levels of lead and zinc protoporphyrin in their blood and high levels of δ-aminolevulinic acid in their urine. These findings indicate considerable lead exposure in the test children's home environments, and demonstrate a need to modify those environments or find a substitute glazing compound that contains no lead. They also confirm again the generally accepted proposition that many population groups dedicated to making ceramic products run a high risk of contracting chronic lead poisoning.

Lead Exposure Among 3-Year-Old Children and Their Mothers Living in a Pottery-Producing Area

Y. Katagiri, H. Toriumi, and M. Kawai. INT ARCH OCCUP ENVIRON HEALTH 1983;52(3):223-9.

Authors' abstract: The present study's aim was to compare the levels of lead exposure between 3-year-old children and their mothers in a pottery-producing area and to assess the levels of lead exposure for 3-year-old children of the parents engaged in pottery-manufacturing work. For these purposes urinary lead, coproporphyrin, and δ-aminolevulinic acid were determined for the children and their mothers living in a pottery-producing area and in a control area. The mean urinary lead was 9.3 to 10.8 μg/l for the mothers in the pottery-producing area and 10.6 μg/l for the children in the control area. In contrast, among the children in the pottery-producing area, those whose parents had been engaged in the pottery production had a much higher mean urinary lead of 13.6 to 15.8 μg/l. These results suggest that parental work related to lead contributes appreciably to lead exposure for children.

Lead Poisoning from Ceramics in the Arab Population

E. Manor and E. Freundlich. ARCH TOXICOL [SUPPL] 1983;6:275-8.

Authors' abstract: Despite the widespread use of handcrafted lead-glazed pottery by the Arab population, no cases of lead intoxication have previously been attributed to these ceramics. Three Arab families were found that used to eat from such earthenware utensils and were afflicted with plumbism. Plumbism was diagnosed by the determination of blood and urine lead levels and, in two of the families, by the decrease of red cell δ-aminolevulinic acid dehydratase activity. The propositus of the first family was the 23-year-old mother, who had abdominal pains and hematuria. Lead intoxication was established and therapy with calcium EDTA instituted. She recovered. Her 1-year-old daughter died in another hospital during a similar episode. Family studies revealed subclinical plumbism in her remaining three sons. In another family, a 54-year-old-man had abdominal pains and a lead line on the gingival margins. Subsequent testing of the surfaces of the earthenware containers from which these families used to eat disclosed excessive amounts of lead. In the third family, eight members had plumbism, four of them with encephalopathy associated with motor palsy. One case was icteric. They also used to eat from primitive pottery with a lead glaze.

White Lead Exposure Among Danish Police Officers Employed in Fingerprint Detection

L. Rabjerg, P.J. Jennum, and H.I. Morck. SCAND J WORK ENVIRON HEALTH 1983 Dec;9(6):511-3.

Authors' abstract: White lead is often used by police officers employed in fingerprint detection (dactylography). On the basis of a case of mild lead intoxication in a police officer, all 22 exposed police officers at the Bureau of Dactylographic Identification in Copenhagen were examined. All went through a clinical examination and blood lead determination. None of the participants showed any sign of lead intoxication. The median blood lead concentration was 0.97 μmol/l (10th-90th percentiles, 0.72-1.44 μmol/l), a value definitely higher than the average of the general population matched for age and sex. A correlation between the weekly white lead exposure and blood lead concentration ($r = 0.87$, $p < 0.0001$) was found among the participants.

Lead Poisoning Among Indian Silver Jewelry Makers

J.R. Behari, S. Singh, S.K. Tandon, and A.K. Wahal. ANN OCCUP HYG 1983;27(1):107-9.

From the text: Nine male silver jewelry makers aged between 25 and 65 yr were suspected of being subject to occupational lead poisoning. Their work involved the purification of silver by heating impure silver together with lead at high temperatures till shining molten silver was obtained. During the process, lead melts and adsorbs the silver impurities, and the entire working atmosphere is filled with smoke laden with lead and lead oxides. The workers are readily exposed to these vapors through inhalation and ingestion. Besides this, the vapors are condensed on the workers' skin and hair and contaminate their clothing, food, and drinking water. The operation lasts from 4 to 6 h each day and for 6 days each week. A concomitant increase in the levels of blood zinc protoporphyrin (ZPP), ZPP/hemoglobin ratio, urinary δ-aminolevulinic acid, and urinary lead with the increase in blood lead concentration was observed. The high concentration of lead vapor in the working environment of Indian jewelry makers without proper exhaust and ventilation seems to be responsible for the symptoms of lead poisoning in at least eight out of nine suspected cases.

A Multivariate Statistical Method for the Establishment of Maximum Allowable Exposure to Toxic Materials in the Workplace

R.B. Goldstein, J.S. Silverberg, and H.F. Martin. AM J IND MED 1984;6(6):459-73.

Authors' abstract: A model has been developed for setting standard limiting concentrations for toxic substances in the body fluid or tissues of industrial workers. The method is very flexible, and it allows the use of either univariate or multivariate data, and of classification schemes that are either supervised, unsupervised, or partially supervised. An index of subclinical biological damage is derived that is used to determine an optimal limiting exposure level. The model is applied to the particular case of selecting a maximum allowable concentration of blood lead in workers in industrial settings where lead toxicity is a danger.

Lead Intoxication. Controlling Lead Exposure in Removal of Old Paint

D. Scott. POSTGRAD MED 1983 Sep;74(3):92-3.

Author's conclusion: Removal of lead-based paint entails a high risk of lead intoxication. This risk can be reduced but cannot be eliminated, even with use of the most aggressive precautions. When a patient reports a history of such activity, the physician should be especially alert to the possibility of lead toxicity. Fatigue, constipation, abdominal pain, and nonspecific neuropsychiatric complaints may all be early signs of lead toxicity. Because the early symptoms are nonspecific, a premium is placed on a careful history.

Home Refinishing, Lead Paint, and Infant Blood Lead Levels

M. Rabinowitz, A. Leviton, and D. Bellinger. AM J PUBLIC HEALTH 1985 Apr;75(4):403-4.

Authors' abstract: We measured the blood lead levels of 249 infants semiannually from birth to 2 years of age; we sampled the home paint and recorded any recent home refinishing activity. Mean blood lead from birth to age 2 years did not vary systematically with age but did correlate significantly with the amount of lead in the indoor paint ($p < .01$). Refinishing activity in homes with high lead paint was associated with elevations of blood lead averaging 69%.

Reproduction and Exposure to Lead

M. Saric. ANN ACAD MED SINGAPORE 1984 Apr;13(2 Suppl):383-8.

Author's abstract: A study on spontaneous abortions and twinning rate was carried out in a commune with a lead smeltery and in a control commune without a specific source of lead exposure. For a period of 20 years (1961-1980) information on spontaneous abortions was recorded from vital statistics data. Data on twin deliveries were obtained from the birth certificates. The additional information regarding sex of twins, maternal age at delivery, and mother's and father's occupations was obtained by an interview. To each twin birth two singleton births were matched by the area of residence and date of birth. Pollution measurements data on lead, zinc, and cadmium were also evaluated. The average annual rate of spontaneous abortions in the commune with a lead smeltery was 12/1,000 and in the control commune, 6.7/1,000 fertile women. The cumulative rate of twin births was 2.4/1,000 inhabitants in the commune with a lead smeltery and 2.6/1,000 inhabitants in the control commune. However, in the commune with a lead smeltery in the area actually exposed to lead, the cumulative rate of twin deliveries over 20 years was 1.7/1,000 inhabitants; in the rest of the commune it was 2.7/1,000 inhabitants. The results indicate a possible interference of lead exposure with reproduction.

Endocrine and Reproductive Dysfunction in Men Associated with Occupational Inorganic Lead Intoxication

M.R. Cullen, R.D. Kayne, and J.M. Robins. ARCH ENVIRON HEALTH 1984 Nov-Dec;39(6):431-40.

Authors' abstract: We attempted to define a postulated effect of lead on male endocrine function in seven men with symptomatic occupational lead intoxication (maximum whole blood lead levels 66-139 μg/dl) who underwent in-patient endocrine evaluation at the time of diagnosis. Defects in thyroid function, probably of central origin, were present in three patients. Six patients had subnormal glucocorticoid production measured by 24-hr urinary 17-hydroxycorticosteroids and plasma cortisol responses to vasopressin- and/or insulin-induced hypoglycemia. Although serum testosterone concentration was normal in six patients, five had defects in spermatogenesis, including two with oligospermia and two with azoospermia. Repeat examinations after chelation therapy showed only partial improvement. It is concluded that heavy occupational exposure to lead, sufficient to cause clinical poisoning, may be associated with diffuse disturbances of endocrine and reproductive functions in men that are not rapidly reversible with standard treatment. Since men without overt poisoning have not been studied, these results cannot yet be included as sequelae of low-dose exposures.

Increased Hair Cadmium in Newborns of Women Occupationally Exposed to Heavy Metals

G. Huel, R.B. Everson, and I. Menger. ENVIRON RES 1984 Oct;35(1):115-21.

Authors' abstract: Newborn and maternal hair samples were obtained from subjects occupationally exposed to heavy metals and from matched controls. The geometric means of levels of cadmium and lead in hair from exposed mothers and of cadmium in hair from transplacentally exposed newborns were twice as high as levels present in samples from controls. There was a positive correlation between levels of cadmium in maternal and newborn hair, but no such correlation for lead. Despite statistically significant evidence of increased exposure to cadmium, no adverse health effects were documented in the small group of exposed newborns included in this study. Problems associated with exogenous contamination of hair by heavy metals and potential advantages of hair sampling for measuring fetal exposures to heavy metals are discussed.

Occupationally Derived Chemicals in Breast Milk

M.S. Wolff. PROG CLIN BIOL RES 1983;117:259-81.

Author's abstract: Exogenously derived chemicals have been widely reported in breast milk. Chemicals typically found in occupational exposures, including trace metals, solvents, and halogenated hydrocarbons, are reviewed in terms of milk partition factors, potential infant exposures, and possible infant health effects. In addition to ingestion of a chemical from breast milk, an infant incurs a neonatal body burden of a chemical because of transplacental migration from maternal blood. For trace metals, neonatal blood levels are similar to maternal blood levels. Partition of metals to milk is

less efficient, but nevertheless can contribute significantly to an infant's body burden. For lipid-soluble pesticide residues and halogenated biphenyls, neonatal body burden is much less than that of the mother, but transfer to milk is efficient because of the high proportion of milk fat. It is suggested that potential organic mercury toxicity can be estimated from concentration in maternal blood or milk. For other chemicals, available data are not sufficient to evaluate short- or long-term health effects. However, for many halogenated hydrocarbons, concentrations in normal human milk would permit infant exposure above guidelines for allowable daily intake set by the World Health Organization.

Dietary Intake of Lead and Blood Lead Concentration in Early Infancy

J.E. Ryu, E.E. Ziegler, S.E. Nelson, and S.J. Fomon. AM J DIS CHILD 1983 Sep;137(9):886-91.

Authors' abstract: Under circumstances of low prenatal exposure to lead and low nondietary exposure to lead postnatally, 4 breast-fed infants and 25 formula-fed infants were studied to determine the relation between dietary intake of lead and blood lead concentration. From 8 through 111 days of age, the mean dietary intake of lead by the formula-fed infants was 17 μg/day (3 to 4 μg/kg/day), and intake of lead by the breast-fed infants was estimated to be only slightly greater. The mean blood lead concentration at the age of 112 days was 6.1 μg/dL. From 112 through 195 days of age, 17 infants continued in the study: 10 received a mean dietary intake of lead of 16 μg/day, and 7 received a mean intake of 61 μg/day. At 196 days of age, mean blood lead concentrations were significantly different (7.2 and 14.4 μg/dL, respectively).

Lead Concentrations of Milk, Blood, and Hair in Lactating Women

S.W. Rockway, C.W. Weber, K.Y. Lei, and S.R. Kemberling. INT ARCH OCCUP ENVIRON HEALTH 1984;53(3):181-7.

Authors' abstract: Lead was measured in the milk of 39 lactating women to determine if the concentration posed a toxicological hazard to nursing infants. Blood and hair of these women were also analyzed for lead to establish possible correlations with milk and to indicate body burdens. The women were categorized as rural or urban residents so that all mean values of lead could then be correlated with their locations. The mean levels of lead in milk, blood, and hair were 3 ng/ml, 119 ng/ml, and 2,002 ng/g (ppb), respectively. Lead levels in milk were not considered high enough to pose any threat to the nursing infant. Furthermore, the levels in blood and hair were below values typically cited as average. The three biological parameters did not correlate significantly with each other or with the location of these women. Therefore, it does not appear that the women in this study have high body burdens of lead, or that the nursing infant is at any risk of lead exposure via milk.

Placental Transfer of Heavy Metals in Normal Pregnant Japanese Women

H. Tsuchiya, K. Mitani, K. Kodama, and T. Nakata. ARCH ENVIRON HEALTH 1984 Jan-Feb;39(1):11-7.

Authors' abstract: To investigate the interrelation of heavy metals and the influence on the next generation, we determined total mercury and methylmercury, lead, cadmium, manganese, copper, zinc, and iron in the maternal blood, placenta, umbilical cord, and umbilical cord blood. Samples were collected at delivery from 231 pregnant women who were living in the city of Nagoya, located in the central district of Japan, during 1974 and 1978. Total mercury and methylmercury, cadmium, and iron were higher in cord blood than in maternal blood, whereas copper and zinc were lower. Significant positive correlations were observed between maternal and cord blood with regard to total mercury and methylmercury, lead, cadmium, and manganese contents. Significant correlations were also observed between many pairs of metals, particularly in umbilical cord and its blood.

Perinatal Lead and Cadmium Burden in a British Urban Population

I.Z. Kovar, C.D. Strehlow, J. Richmond, and M.G. Thompson. ARCH DIS CHILD 1984 Jan;59(1):36-9.

Authors' abstract: Concentrations of the potential pollutants, lead and cadmium, were studied in the perinatal period in a British urban population. Blood lead and cadmium concentrations and iron status were measured in 28 mother and infant pairs at delivery and at 5 days postpartum in the mother; breast milk collected at 5 days postpartum under controlled conditions was analyzed for lead and cadmium. Placental transfer of both metals was noted; concentrations of lead in breast milk (mean concentration 0.01 mmol/l (2 μg/l) were less than in two brands of commercial prepacked formulas, and the concentrations of cadmium in breast milk and prepacked formulas (mean 3.6 nmol/l (0.4 μg/l] were similar. The risk of excess lead or cadmium intake from breast milk is small.

Urban Lead Levels in Minneapolis: The Case of the Hmong Children

H.W. Mielke, B. Blake, S. Burroughs, and N. Hassinger. ENVIRON RES 1984 Jun;34(1):64-76.

Authors' abstract: In this study, soil lead is used as a means of describing the urban lead levels in the metro-

politan area of the Twin Cities, and the soil lead levels next to homes of neighborhoods of the metropolitan area are assessed. Lead levels of rural soils are around 5 μg/g. Near the city limits they increase to 25-50 μg/g, and in the central business district they are around 500 to 1,000 μg/g, or over 100 times greater than in the rural areas. Many Hmong children are suffering from undue lead absorption. The homes of the Hmong children were all located in inner-city neighborhoods. Soil around these homes was compared with soils around homes of a neighborhood away from the inner city. Fifty percent of the Hmong children with lead poisoning inhabit homes that have soil lead levels of 500-999 μg/g, and 40% live in homes with lead levels of 1,000 μg/g or more. One home of ten in the outer city has soil lead levels above 500 μg/g. The lead sources of the inner city include house paint and leaded gasoline from vehicle traffic. Raising children in high-lead environments as found in the Minneapolis inner city has long-term implications because of mental and behavioral deficits that are known to result from chronic exposure to lead.

Lead Concentrations in Inner-City Soils as a Factor in the Child Lead Problem

H.W. Mielke, J.C. Anderson, K.J. Berry, P.W. Mielke, R.L. Chaney, and M. Leech. AM J PUBLIC HEALTH 1983 Dec;73(12):1366-9.

Authors' abstract: Soil samples were randomly collected from 422 vegetable gardens in a study area centered in downtown Baltimore, Maryland, and having a radius of 48.28 km (30 miles). The levels of lead, four other metals (cadmium, copper, nickel, and zinc), and pH were measured for each location. The application of multiresponse permutation procedures, which are compatible with mapping techniques, reveals that lead (as well as cadmium, copper, nickel, and zinc) is concentrated and ubiquitous within the soils of the inner-city area of Metropolitan Baltimore. The probability values that the concentration of metals occurred by chance alone vary from about 10^{-15} to 10^{-23} depending on the metal considered. Our findings pose environmental and public health issues, especially to children living within the inner city.

Dietary Lead Intake of Preschool Children

L.K. Bander, K.J. Morgan, and M.E. Zabik. AM J PUBLIC HEALTH 1983 Jul;73(7):789-94.

Authors' abstract: A nationwide, 7-day food consumption survey of 371 preschool children between the ages of birth and 5 years indicated that a direct linear relationship existed between age and increased dietary lead intake from foods consumed. Daily dietary lead intake averaged 62 μg and ranged from 15 μg to 234 μg. The various levels of lead intake were attributed to frequency of consumption of food items, quantity of food consumed, and the lead content of particular food items. To account for variation in the quantity of food consumed by the various children, we calculated average lead intake per 500 kilocalories consumed and per 500 g of food consumed. When these standardization procedures were followed, an equalization in the average daily dietary lead intake values was observed among the children of various ages.

The Intake and Excretion of Lead and Cadmium by the Elderly

V.W. Bunker, M.S. Lawson, H.T. Delves, and B.E. Clayton. AM J CLIN NUTR 1984 May;39(5):803-8.

Authors' abstract: Metabolic balances for lead and cadmium were carried out in 23 healthy elderly people aged 69.7 to 85.5 yr while living in their own homes and eating self-selected diets. Mean intakes of lead and cadmium were 54.6 and 8.6 μg/day, with mean retentions of −8.7 and −1.7 μg/day, respectively. Daily dietary lead correlated ($p < 0.05$) with the intake of energy, nitrogen, calcium, iron, and zinc but not with manganese or copper. Dietary intake of cadmium correlated ($p < 0.05$) only with that of zinc and manganese. There was a highly significant ($p < 0.001$) inverse correlation between the percentage cadmium absorbed and body iron stores measured as serum iron, percentage iron saturation, and ferritin. Mean whole blood concentrations were 138 μg/l for lead and 0.79 μg/l for cadmium. The negative balances observed in these elderly people were very different from the positive balances found in a previous similar study in children.

A Tentative Classification of Agricultural Foods Exposed to Roadside Lead Contamination

L.G. Favretto. Z LEBENSM UNTERS FORSCH 1984 Jun;178(6):450-2.

Author's abstract: A systematic study of vegetables and other agricultural products used as foods was performed to suggest a tentative classification of products exposed to roadside lead pollution from automobile exhausts. A hyperbolic two-parameter function is used as an empirical model to describe the decrease in lead content with the distance from the line source. Regression analysis of the linearized function allows the estimation of the parameters. Polluted products are classified by means of cluster analysis.

Vegetable Consumption and Blood Lead Concentrations

J.E. Gallacher, P.C. Elwood, K.M. Phillips, B.E. Davies, R.C. Ginnever, C. Toothill, and D.T. Jones. J EPIDEMIOL COMMUNITY HEALTH 1984 Jun;38(2):173-6.

Authors' abstract: Women residing in an area heavily contaminated by spoil from old lead mining have blood lead concentrations that are about 50% higher ($p < 0.001$) than those of women living in a "control" area some distance away. Blood lead concentrations were related to the consumption of home-grown produce. Those with the highest consumptions had blood lead concentrations that were 28% higher ($p < 0.001$) than those of women who consumed no locally grown vegetables. Nevertheless, in the total population in the area this effect seemed likely to account for only about 5% of the population mean blood lead concentration. The data suggested that an increase in soil lead of 1,000 μg/g is associated with an increase in blood lead of about 0.20 μM/l (4.2 μg/dl).

Lead Uptake from Vegetables Grown Along Highways

M. Wijn, P. Duives, R. Herber, and B. Brunekreef. INT ARCH OCCUP ENVIRON HEALTH 1983;52(3):263-70.

Authors' abstract: Blood-lead (PbB) levels were measured in tenants of vegetable gardens located close to busy highways (average: > 25,000 vehicles per workday) in the Netherlands. For comparison, PbB levels were determined in tenants of vegetable gardens located away from busy traffic. The results indicate that there is no significant difference between the geometric mean PbB levels of the two populations, despite a twofold to threefold difference in the lead content of their vegetables and despite frequent consumption of these vegetables in the exposed group. Mean PbB values were around 0.48 μmol/l (100 μg/l), which is well below existing health guidelines and slightly below the levels found in another recent survey of Dutch suburban residents.

Cadmium and Lead Through an Agricultural Food Chain

E. Brams and W. Anthony. SCI TOTAL ENVIRON 1983 Jun;28:295-306.

Authors' abstract: In two experiments, quantities of soil cadmium (Cd) and lead (Pb) were measured in wheat grain and eggs of laying hens that ingested the grain for 34 days and in liver and muscle after a 30-day withdrawal period. Soil Cd (0.6 to 2.9 ppm) induced a direct and linear accumulation in grain, which ranged from 1.25 to 5.36 ppm. No response to soil Pb (4.0 to 18.7 ppm) was detected in grain, which averaged 2.7 ± 1.5 ppm. Ingestion by hens of 1,500 to 11,000 μg Cd/kg body wt induced 1.87 ppm in dry albumin, but Cd was not detectable in yolk, liver, or muscle. Lead ingested after 34 days averaged 13,386 μg/kg body wt and induced a mean of 3.88 and 4.71 μg Pb/g in yolk and albumin, respectively, but none in liver and muscle. From the soil pool 0.004% Cd and 0.02% Pb accumulated in the grain; 1.6% of grain Cd accumulated in the eggs. Only minuscule quantities (1×10^{-5}) of the Cd and Pb in the soil pool were transferred and retained in hen tissues via ingestion of the grain.

Lead Content of Water and of Reconstituted Infant Formula in Vienna

F. Haschke, I. Steffan, R. Schilling, E. Schuster, and H.P. Salzer. MINER ELECTROLYTE METAB 1985;11(1):45-51.

Authors' abstract: Daily lead intake from infant formula was estimated for young infants living in Vienna on the basis of determinations of the lead concentration of drinking water and powdered formulas. The lead concentration in water was higher in houses built before 1945 (median, 15.6 μg/l) than in houses built between 1945 and 1965 (median, 4.4 μg/l) and in houses built after 1965 (median, 2.8 μg/l). Boiling water for 1 min substantially reduced ($p < 0.0005$) the lead concentration in water from all houses, apparently because of the coprecipitation of lead with boiler scale. The mean lead concentration in infant formula powder ($n = 36$) was 161.8 (SD 103.7) μg/kg. The lead concentration of an "average" reconstituted infant formula, calculated by using the mean lead concentration of boiled water (5.4 μg/l) and of formula powder, was 27.5 μg/l. This corresponded to 4.1 μg/100 kcal, which was substantially below the FDA maximum value of 16 μg/100 kcal. The lead concentration in the fat-free mass of a hypothetical young infant was estimated, assuming formula as the only source of lead and average values for caloric intake and retention of ingested lead. Between 0 and 4 months the estimated lead concentration in the fat-free mass declined from the concentration present at birth, indicating that the lead intake from formula is not likely to cause lead accumulation in the body during early infancy.

Trace Metals in Drinking Water: Lack of Influence on Blood Pressure

D. Sparrow, A.R. Sharrett, A.J. Garvey, G.F. Craun, and J.E. Silbert. J CHRONIC DIS 1984;37(1):59-65.

Authors' abstract: It has been suggested that certain trace metals may affect human blood pressure. We

recently measured trace metals in the tapwater from the homes of 246 male participants of the Normative Aging Study. Participants were free of any disease or medication known to influence blood pressure. No statistically significant relationship was found between lead concentration and systolic blood pressure in an analysis of covariance, controlling for age and body mass index. Diastolic pressure was examined as well and the results were almost identical. Since educational level and town of residence were potential confounders, we stratified on these variables, but no association between lead concentration and blood pressure emerged. Similarly, no statistically significant relationships were found between blood pressure and copper or iron. Blood pressure did differ significantly among zinc concentration groups, but no uniform trend appeared. In light of evidence from other studies suggesting that blood pressure is influenced by lead or other elements in drinking water, further investigations with more highly exposed subjects or a prospective design appear warranted.

Reduction in Exposure to Lead from Drinking Water and Its Effect on Blood Lead Concentrations

J.C. Sherlock, D. Ashby, H.T. Delves, G.I. Forbes, M.R. Moore, W.J. Patterson, S.J. Pocock, M.J. Quinn, W.N. Richards, and T.S. Wilson. HUM TOXICOL 1984 Oct;3(5):383-92.

Authors' abstract: The water supply in Ayr (Scotland, UK) was plumbosolvent, and many dwellings in Ayr contained lead pipes. In 1981, treatment of the water supply to reduce its plumbosolvency was initiated. Measurements of water and blood lead concentrations were made before and after the treatment. Most of the measurements made before and after water treatment began were made on water samples from the same dwellings and blood samples from the same women. Water treatment produced a sharp fall in water lead concentrations and a decrease in the median blood lead concentration from 21 to 13 μg/100 ml. Two women had higher than expected blood lead concentrations; both these women had been removing old paint. Women who had lead pipes removed from their dwellings all showed substantial decreases in their blood lead concentrations. The curvilinearity of the relation between blood lead and water lead concentrations is confirmed. Even relatively low (< 40 μg/l) water lead concentrations may make a substantial contribution to blood lead concentrations.

Intakes of Copper, Zinc, Cadmium, Tin, Iron, Nickel and Arsenic in a Population Exposed to Lead from Water

J.C. Sherlock, G.A. Smart, J.I. Read, P.J. Brooke, G. Forbes, W. Patterson, W. Richards, M. Moore, and T. Wilson. SCI TOTAL ENVIRON 1983 Sep;30:255-60.

Authors' abstract: Adult diets obtained from a population in Ayr, Scotland, United Kingdom, known to be exposed to lead from water were analyzed for arsenic, cadmium, copper, iron, nickel, tin, and zinc to assess the intake of these elements. With few exceptions, the concentration of each element varied little from diet to diet, and therefore the range of intakes varied only in proportion to the weights of the diets. With the exception of nickel, the difference between the observed average dietary intakes of the metals studied and those expected on the basis of a nationwide Total Diet Study is largely accounted for on the basis of the differences between the weights of the duplicate diet and the weight for the Total Diet Study.

Studies of Lead and Cadmium Exposure in Glasgow, U.K.

M.J. McIntosh, M.R. Moore, A. Goldberg, G.S. Fell, C. Cunningham, and D.J. Halls. ECOL DIS 1982;1(2-3):177-84.

Authors' abstract: Domestic water and whole blood samples were collected early in 1981 from 200 volunteers living in the Glasgow area of Scotland, U.K. The concentration of lead in the water and blood samples, and of cadmium in the blood, was measured. The blood lead and cadmium concentrations were compared with those obtained in the Survey of 1979. There has been a fall in blood lead concentrations since the 1979 Survey. In contrast, the blood cadmium levels had remained similar. This diminution in blood lead concentration is attributed to a fall in water lead concentration caused by raising the pH of the water supply in the Glasgow area. The main determinant for cadmium in blood appears to be cigarette smoking habits, which had not changed.

Greater Contribution to Blood Lead from Water than from Air

P.C. Elwood, J.E. Gallacher, K.M. Phillips, B.E. Davies, and C. Toothill. NATURE 1984 Jul 12-18;310(5973):138-40.

Authors' abstract: Concern about the levels of lead in blood is widespread. There is uncertainty, however, about the relative importance of the various environmental sources. Lead in petrol is widely assumed to be one of the most important sources, and air and dust have been identified as the main routes to man. Water is regarded as

an important source in areas with a plumbosolvent water supply, but of little or no importance in other areas. To evaluate the contribution to blood lead by various environmental sources, we have conducted surveys of random samples of women in areas of Wales chosen to represent very different levels of exposure to traffic. We report here that lead in air makes a small, but significant, contribution to blood lead, but there is no evidence of any contribution from dust. Although in none of the areas were high levels of lead detected in water, water emerges as an important contributor to blood lead.

Hardness of Domestic Water and Blood Lead Levels

P.C. Elwood, K.M. Phillips, N. Lowe, J.K. Phillips, and C. Toothill. HUM TOXICOL 1983 Oct;2(4):645-8.

Authors' abstract: The effect on the blood lead levels of residents in an area in which a soft plumbo-solvent water was hardened is examined. Water lead levels fell after hardening was introduced, whereas there was a small rise in water lead levels in a control area monitored over the same time. The blood lead levels of residents fell after hardening, and the fall was slightly greater than would have been predicted on the basis of the change in water lead levels. This suggests that lead is less well absorbed from hard water than from soft water. Following hardening there was a significant fall in mean blood lead level of subjects living in houses that had initially had negligible amounts of lead in the water. This suggests that hard water may interfere with the absorption of lead from sources other than water.

Lead Toxicity from Water (Letter)

J. Gallacher, L. Harris, and P.C. Elwood. NATURE 1983 Sep 22-28;305(5932):280.

From the text: Several studies suggest a curvilinear relationship between water lead and blood lead. Hard water may reduce the absorption of lead from sources other than water, such as food. A random sample of women stratified by water lead level in a plumbosolvent area showed a reduction of blood lead with hardening of water. A reduction in blood lead was shown even where initial water lead levels were negligible; no reduction was shown in a nearby area where water was not hardened. In general, the highest blood lead levels seem to occur in soft water areas, so our data suggest that the hardening of soft water supplies could make a substantial contribution to the general reduction of blood lead in this country.

Contribution of Lead in Dust to Children's Blood Lead

M.J. Duggan. ENVIRON HEALTH PERSPECT 1983 Apr;50:371-81.

Author's abstract: The importance of urban dust as a source of lead for young children is still disputed. Although blood-lead data from various population surveys usually show a peak concentration in early childhood, there is evidence that such a peak is small or absent altogether in children without much access to the general environment. An examination of those studies where groups of people in regions of low and high lead contamination have been compared shows that the child/adult blood-lead ratio is almost always enhanced in the more exposed groups. This implies a route of lead uptake that is important for children but less so for adults, and it is likely that this route is the dust-hand-mouth one. There are sufficient data to suggest a quantitative relationship between raised levels of blood lead and lead in dust. There is a strong case for a lead-in-dust standard, but some will probably remain unpersuaded unless or until there are reliable data for blood lead and environmental lead involving matched groups of young people from urban and rural areas.

Childhood Lead Poisoning. A Controlled Trial of the Effect of Dust-Control Measures on Blood Lead Levels

E. Charney, B. Kessler, M. Farfel, and D. Jackson. N ENGL J MED 1983 Nov 3;309(18):1089-93.

Authors' abstract: Lead-contaminated house dust is one factor in childhood lead poisoning; however, most lead-reduction programs do not emphasize the control of house dust. We studied whether lead-reduction plus dust-control measures would lower blood lead levels in children with Class II or III poisoning (blood lead levels, 30 to 49 μg/dl) more effectively than lead reduction alone. An experimental group of 14 children and a control group of 35 children whose homes had already been treated were studied. In experimental homes, sites with elevated lead levels ($>$ 100 μg per 930 cm^2) were wet-mopped twice monthly and families were encouraged to clean and to wash the child's hands frequently. After 1 year blood lead levels fell an average of 6.9 μg/dl in the experimental group, as compared with 0.7 μg/dl in controls ($P < 0.001$). Children in the experimental group with the highest blood lead levels had the most marked reduction. Four children in the control group (and none in the experimental group) required chelation therapy for blood levels $>$ 50 μg/dl. These results show that a focused dust-control program can reduce blood lead levels more than standard lead removal in the home.

The Relationship Between Air Lead and Blood Lead in Children: A Critical Review

B. Brunekreef. SCI TOTAL ENVIRON 1984 Sep;38:79-123.

Author's abstract: A review is given of community studies from which the relationship between air lead and

blood lead in children of varying ages can be estimated. The review covers 19 different studies that were carried out in 10 different countries. The blood lead/air lead relationship is denoted with the symbol "α." It is concluded that, for children, a wide range of α-values can be estimated from the data in the different studies. Most values center on 3-5 rather than the 1-2 that is usually reported from adults. However, adjustment for confounders has been absent or incomplete in most, if not all, studies. Most α-estimates thus have to be viewed with caution.

A Comparative Study of Air-Borne Lead Affecting Different Bangkok Civilian Population Groups

C. Chaikittiporn, S. Yoosook, W. Yoosook, A. Soonthornpong, M. Rojnajin, A. Rangsitiyakorn, U. Kongmueng, C. Banpenyoo, and S. Anantame. J MED ASSOC THAI 1983 Jun;66 Suppl 1:49-53.

Authors' summary: The level of particulates and lead content in the air breathed by people in various areas of Bangkok was investigated. The blood lead level of different occupational groups was also examined. Air samples were collected from 17 major street intersections by two methods: (1) general air sampling, using fixed sampling stations and (2) respiratory zone air sampling, using personal dust sampler on traffic policemen. Results of respiratory zone samples analysis showed an average particulate concentration of 0.6170 mg/m^3 and average lead concentration of 4.6432 μg/m^3. General air samples showed average concentrations of 0.4151 mg/m^3 and 5.0651 μg/m^3, respectively. Analysis of 549 blood samples indicated differences of lead content level between various occupational groups. The highest level was found among taxi and motor-tricycle drivers (0.0445 mg/100 g) and traffic policemen (0.043 mg/100 g). Normal blood levels of people in rural areas in the north and northeast were 0.0244 and 0.0275 mg/100 g, respectively. Significant differences of blood lead levels were found between the following groups (higher level in the first group): smokers and nonsmokers; male and female; people who spend more time in the streets and those who spend less time, including older and younger persons.

Measurement of ^{210}Pb Atmospheric Flux in the Pacific Northwest

A.E. Nevissi. HEALTH PHYS 1985 Feb;48(2):169-74.

Author's abstract: Monthly atmospheric flux of ^{210}Pb in Seattle, Washington, has been measured over a period of 7 yr. Direct correlation exists between monthly rainfall and the ^{210}Pb deposition; however, for the same amount of rainfall the ^{210}Pb deposition varies from year to year. The mean annual input of ^{210}Pb is 0.44 dpm/cm^2, and the standard error of the mean is ± 0.24 dpm/cm^2. A 4.4-fold fluctuation in the ^{210}Pb annual flux was observed during this investigation.

Relationship Between the ^{210}Pb Content of Teeth and Exposure to Rn and Rn Daughters

G.F. Clemente, A. Renzetti, G. Santori, F. Steinhausler, and J. Pohl-Ruling. HEALTH PHYS 1984 Aug;47(2):253-62.

Authors' abstract: Existing data on ^{210}Pb in human teeth are reviewed for various countries. The mean value of ^{210}Pb in the teeth of population groups exposed to "normal" levels of radon-daughter exposure is about 2 mBq/g. A detailed analysis of 48 samples from a "normal" Italian population group revealed that smoking habits and age may have some influence on ^{210}Pb content of teeth, although this is not the case for differences in sex. A group of 45 Austrians exposed to elevated levels of radon and radon daughters is compared with the Italian group. After background levels of ^{210}Pb as found for the normal Italian population were subtracted, the incremental ^{210}Pb tooth content due to excessive radon-daughter exposure has been correlated with the individual cumulative exposure corrected for background radon-daughter exposure. A statistical analysis shows the significance of the linear correlation at the $\alpha = 0.01$ level. For the incremental increase of ^{210}Pb in teeth, a value of 1.2 mBq/g has been used for a lifetime exposure to 1 WLM. This result is compared with corresponding data published in the literature, which are predominantly related to the ^{210}Pb content of bone after short-time exposure at high levels, e.g., in uranium mines. The comparison seems to indicate the influence of the exposure rate and the need for a comprehensive model that takes into account radon-daughter inhalation, radon dissolved in body fluids, and ^{210}Pb metabolism.

Lead Levels in Deciduous Teeth of Queensland Children

D.E. Clegg, I.W. Eddington, P.J. McKinnon, and M.D. Sheumack. MED J AUST 1984 Oct 27;141(9):590-3.

Authors' abstract: Lead levels in the deciduous teeth of 292 Queensland children, aged between 4 and 9 years, are reported. Samples were obtained through the cooperation of parents of children attending kindergartens throughout the State in 1981. Information relating to the child's place of residence, home environment, and parents' occupation was also gathered with the aid of a questionnaire. Tooth lead levels ranged from 0 to 29 μg/g (mean, 3.4 μg/g; SD, 4.1 μg/g). Possible relationships between aspects of the subject's history and lead levels are discussed, and the data are compared with those of similar, already published studies.

Lead Content of Deciduous Molar Enamel in Finland, as Measured by Proton-Induced X-Ray Emission

V. Jarvinen, A. Anttila, R. Lappalainen, and I. Rytomaa. SCAND J WORK ENVIRON HEALTH 1984 Apr;10(2):103-7.

Authors' abstract: The lead content of deciduous molar enamel was measured with an accurate physical technique based on proton-induced X-ray emission. The absolute values were calibrated according to the animal bone standard of the International Atomic Energy Agency. The results obtained from five different communities indicated little difference between communities in the lead content of the deciduous molar enamel of children born in 1960-1975. The overall mean for all samples analyzed was 3.2 (SD 1.6) μg/g (N = 120); the highest individual value measured was 10.0 μg/g. Judging from the lead content of the teeth, the general population in Finland does not yet seem to be exposed to detectably higher amounts of artificially occurring environmental lead, neither in urban nor in rural areas. It would seem that naturally occurring environmental lead still plays a decisive role in the integrated long-term exposure in Finland.

Lead Concentrations of Enamel and Dentine of Deciduous Teeth of Children from Two Finnish Towns

K. Haavikko, A. Anttila, A. Helle, and E. Vuori. ARCH ENVIRON HEALTH 1984 Mar-Apr;39(2):78-84.

Authors' abstract: The proton-induced x-ray emission method was used to analyze lead concentrations in enamel and dentine of deciduous teeth of 105 6- and 9-yr-old children living in two Finnish towns. Helsinki, the capital city, was assumed to represent high lead exposure and Kuopio, a country town in the middle of Finland, low or moderate lead exposure. In all but two teeth the enamel contained higher lead concentrations than dentine. The individual enamel-dentine lead concentration ratio was not stable but varied greatly. The median dentine lead concentration for 9-yr-old children in Helsinki and Kuopio was 2.0 ppm and 2.9 ppm, respectively, and for 6-yr-old children was 2.5 ppm and 2.7 ppm, respectively. The enamel lead concentrations found in 9-yr-olds in Helsinki and Kuopio were 4.2 and 4.5 ppm, and in 6-yr-olds were 9.1 and 4.4 ppm, respectively. The results reveal low or moderate lead concentrations. Nevertheless, a twofold and statistically significant ($P < .01$) increase was found in the enamel of Helsinki children born in 1974 compared with those born in 1971.

Lead Levels in Deciduous Teeth of Children from Selected Urban Areas in the Cape Peninsula

C.W. van Wyk and S.R. Grobler. S AFR MED J 1983 Apr 9;63(15):559-62.

Authors' abstract: The lead levels in shed deciduous teeth of children from two selected urban regions in the Cape Peninsula were compared. The average levels in the teeth of children living in the vicinity of two large industrial plants were: whole teeth, 20,419 ppm; enamel, 10,952 ppm; and dentine, 22,733 ppm. The lead levels in teeth from children living in the vicinity of light industries were: whole teeth, 16,556 ppm; enamel, 2,919 ppm; and dentine, 19,926 ppm. These differences were significant at the 1% level (teeth and enamel) and 5% level (dentine).

Comparative Studies on the Distribution of Heavy Metals in the Oceans and Coastal Waters

L. Mart, H. Rutzel, P. Klahre, L. Sipos, U. Platzek, P. Valenta, and H.W. Nurnberg. SCI TOTAL ENVIRON 1982 Dec;26(1):1-17.

Authors' abstract: Results of our investigations during the last 5 years are summarized. The concentrations of Cd, Pb, and Cu have been determined in coastal areas of the Western Mediterranean and the North Sea; this reflects the influence of the pollution sources along the shore line. Deep sea water and surface water samples from the Pacific, Atlantic, Mediterranean, and Arctic Sea have been analyzed for Cd, Pb, Cu, and at some stations also for Ni and Co. It is demonstrated that concentration levels of surface and deep sea waters may differ significantly in diverse oceans. The same is valid to a greater extent for coastal waters affected particularly by anthropogenic input that can be dispersed by tidal currents. Applying reliable sampling methods, and the voltammetric determination procedure in particular, suitable for heavy metals at the trace level, we could achieve significant contributions to a consistent data basis for the distribution of heavy metals in the sea.

Lead Burden in Mute Swans from Denmark

B. Clausen, K. Elvestad, and O. Karlog. NORD VET MED 1982 Mar;34(3):83-91.

From authors' abstract: During the severe winter of 1978-79, large numbers of mute swans died in coastal areas in Denmark; of these, 2,111 were collected for autopsy. The area of origin and the sex of the 2,111 swans, 184 of which were ringed, are given. At autopsy most of the swans were recorded as having died from starvation. Lead pellets were found in only 0.7% of the gizzards, probably because most ingested pellets had been eroded away before the swans died. The results of analysis of 76

swans selected at autopsy and of the 184 ringed swans show that lead-poisoned swans are not always recognized at autopsy. Ten per cent of the ringed swans carried more than 7 mg lead per kg liver wet weight (Ww) and 34% more than 3 mg/kg (Ww), and an elevated lead content (> 30 mg/kg dry weight) was found in the sternum of 40% of the swans. The load of lead in the liver was higher in the few swans from the western part of Jutland than in swans from the main sampling areas, whereas in the sternum it was relatively lower in swans from the southern part of the country (Lolland, Falster). No difference in lead content was found between males and females. The lead content in the liver was not correlated with age, but a positive correlation was found between age and the lead content in the sternum.

Heavy Metals (Copper, Cadmium, Lead, Mercury) in Mute Swans from Denmark

K. Elvestad, O. Karlog, and B. Clausen. NORD VET MED 1982 Mar;34(3):92-7.

Authors' abstract: During the severe winter of 1978-79, large numbers of mute swans died in coastal areas of Denmark. Of these, 2,111 were collected for examination. The analyses confirm previous findings of relatively high copper levels in mute swans (mean for 178 livers was 2,680 mg/kg dry weight (Dw) and for 110 kidneys 34 mg/kg Dw). The copper content was not related to sex or age. The highest liver levels of copper were found in swans from Western Jutland. Cadmium was found at the same relatively low levels as recorded for waterfowl elsewhere (mean for 178 livers was 12 mg/kg Dw, for 110 kidneys 24 mg/kg Dw). The cadmium content was not sex related, but it increased with age. The mean mercury content (liver) was 1.4 mg/kg Dw in the 10 birds analyzed. The mean lead content was 15 mg/kg Dw in the 178 livers analyzed and 31 mg/kg Dw in 110 sternums. The lead content was not sex related. In sternums, but not in livers, it was related to age. One third of the swans were found to be lead contaminated, probably after ingestion of lead pellets. None of the swans carried high levels of both copper, cadmium, and lead.

Multiple Causes of Anaemia Amongst Children Living Near a Lead Smelter in Brazil

F.M. Carvalho, M.L. Barreto, A.M. Silvany-Neto, H.A. Waldron, and T.M.Tavares. SCI TOTAL ENVIRON 1984 Apr 5;35(1):71-84.

Authors' abstract: A prevalence study of anemia was carried out amongst children, aged 1 to 9 years, living near a lead smelter in Santo Amaro City, Northeast Brazil. The variation in hemoglobin levels was found to be significantly associated with malnutrition and with the interaction between malnutrition and iron deficiency, but not with lead poisoning, iron deficiency, or hookworm infection, having allowed for the effects of age, area of residence, family per capita income, and race. The effect of the interaction between malnutrition and iron deficiency on hemoglobin levels was most prominent amongst children aged 1 year and amongst those living in the most deprived area. The lack of demonstrable interaction between lead poisoning and iron deficiency in the causation of anemia amongst these children is discussed.

Lead Poisoning and Hookworm Infection as Multiple Factors in Anaemia

S. Loureiro, A.G. Spinola, F.M. Carvalho, and M.L. Barreto. TRANS R SOC TROP MED HYG 1983;77(3):321-2.

Authors' abstract: A retrospective study was carried out in a rural area of northeastern Brazil, to search for interactions between biological and chemical agents present in the environment as causes of anemia. A lead smelter situated in a hookworm endemic area provided the opportunity to look at the effect of this double exposure in relation to laboratory-defined anemia, by comparing the odds ratios in different subgroups of 109 "cases" and 107 "controls." The subgroup with both hookworm infection and chronic lead poisoning—measured by the concentration of δ-aminolevulinic acid (ALA) excreted in urine—had an odds ratio of developing anemia five times greater than individuals with neither. Although a synergistic effect could not be demonstrated, the additive effect of the two conditions placed this group in a higher risk category.

SELECTED BIBLIOGRAPHY

*Abdullah MA. Lead poisoning among children in Saudi Arabia. J TROP MED HYG 1984 Apr;87(2):67-70.

Ackerman A, Rodman D. Azarcon and empacho [letter]. PEDIATRICS 1984 Jan;73(1):114-5.

*Angle CR, Marcus A, Cheng IH, McIntire MS. Omaha childhood blood lead and environmental lead: a linear total exposure model. ENVIRON RES 1984 Oct;35(1):160-70.

Anonymous. Lead in petrol: a long farewell [editorial]. LANCET 1983 Apr 23;1(8330):912.

Arnot R. Lead in paint [letter]. J R SOC HEALTH 1984 Dec;104(6):232.

*Bander LK, Morgan KJ, Zabik ME. Dietary lead intake of preschool children. AM J PUBLIC HEALTH 1983 Jul;73(7):789-94.

Barish RJ. Evaluation of lead releases from the burning of lead acrylic x-ray shielding. HEALTH PHYS 1984 Feb;46(2):464-6.

*Beazley WC, Rosenthal RE. Lead intoxication 18 months after a gunshot wound. CLIN ORTHOP 1984 Nov;(190):199-203.

*Behari JR, Singh S, Tandon SK, Wahal AK. Lead poisoning among Indian silver jewelry makers. ANN OCCUP HYG 1983;27(1):107-9.

*Bose A, Vashistha K, O'Loughlin BJ. Azarcon por empacho—another cause of lead toxicity. PEDIATRICS 1983 Jul;72(1):106-8.

*Brams E, Anthony W. Cadmium and lead through an agricultural food chain. SCI TOTAL ENVIRON 1983 Jun;28:295-306.

*Brodeur J, Lacasse V, Talbot D. Influence of removal from occupational lead exposure on blood and saliva lead concentrations. TOXICOL LETT 1983 Oct-Nov;19(1-2):195-9.

*Brunekreef B. The relationship between air lead and blood lead in children: a critical review. SCI TOTAL ENVIRON 1984 Sep;38:79-123.

Brunekreef B, Noy D, Biersteker K, Boleij J. Blood lead levels of Dutch city children and their relationship to lead in the environment. J AIR POLLUT CONTROL ASSOC 1983 Sep;33(9):872-6.

Budiansky S. Gasoline lead: Ruckelshaus makes a move [news]. NATURE 1984 Aug 16-22;310(5978):532.

*Bunker VW, Lawson MS, Delves HT, Clayton BE. The intake and excretion of lead and cadmium by the elderly. AM J CLIN NUTR 1984 May;39(5):803-8.

Caplun E, Petit D, Picciotto E. Lead in petrol. ENDEAVOUR 1984;8(3):135-44.

*Carvalho F, Tavares TM, Souza SP, Linhares PS. Lead and cadmium concentrations in the hair of fishermen from the Subae River basin, Brazil. ENVIRON RES 1984 Apr;33(2):300-6.

*Carvalho FM, Barreto ML, Silvany-Neto AM, Waldron HA, Tavares TM. Multiple causes of anaemia amongst children living near a lead smelter in Brazil. SCI TOTAL ENVIRON 1984 Apr 5;35(1):71-84.

Centers for Disease Control. Lead poisoning-associated death from Asian Indian folk remedies—Florida. MMWR 1984 Nov 16;33(45):638, 643-5.

Centers for Disease Control. Lead poisoning from Mexican folk remedies—California. MMWR 1983 Oct 28;32(42):554-5.

Centers for Disease Control. Reducing exposures to airborne lead in indoor firing ranges—United States. MMWR 1983 Sep 23;32(37):483-4, 489.

*Chaikittiporn C, Yoosook S, Yoosook W, Soonthornpong A, Rojnajin M, Rangsitiyakorn A, Kongmueng U, Banpenyoo C, Anantame S. A comparative study of air-borne lead affecting different Bangkok civilian population groups. J MED ASSOC THAI 1983 Jun;66 Suppl 1:49-53.

*Charney E, Kessler B, Farfel M, Jackson D. Childhood lead poisoning. A controlled trial of the effect of dust-control measures on blood lead levels. N ENGL J MED 1983 Nov 3;309(18):1089-93.

Chau YK, Wong PT, Bengert GA, Dunn JL. Determination of dialkyllead, trialkyllead, tetraalkyllead, and lead(II) compounds in sediment and biological samples. ANAL CHEM 1984 Feb;56(2):271-4.

*Chavalitnitikul C, Levin L, Chen LC. Study and models of total lead exposures of battery workers. AM IND HYG ASSOC J 1984 Dec;45(12):802-8.

*Chisolm JJ Jr. The continuing hazard of lead exposure and its effects in children. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):23-42.

*Clausen B, Elvestad K, Karlog O. Lead burden in mute swans from Denmark. NORD VET MED 1982 Mar;34(3):83-91.

*Abstracted

*Clegg DE, Eddington IW, McKinnon PJ, Sheumack MD. Lead levels in deciduous teeth of Queensland children. MED J AUST 1984 Oct 27;141(9):590-3.

*Clemente GF, Renzetti A, Santori G, Steinhausler F, Pohl-Ruling J. Relationship between the ^{210}Pb content of teeth and exposure to Rn and Rn daughters. HEALTH PHYS 1984 Aug;47(2):253-62.

*Craft AW. Circumstances surrounding deaths from accidental poisoning 1974-80. ARCH DIS CHILD 1983 Jul;58(7):544-6.

*Cullen MR, Kayne RD, Robins JM. Endocrine and reproductive dysfunction in men associated with occupational inorganic lead intoxication. ARCH ENVIRON HEALTH 1984 Nov-Dec;39(6):431-40.

*Dalpra L, Tibiletti MG, Nocera G, Giulotto P, Auriti L, Carnelli V, Simoni G. SCE analysis in children exposed to lead emission from a smelting plant. MUTAT RES 1983 Jun;120(4):249-56.

*Davies JM. Long-term mortality study of chromate pigment workers who suffered lead poisoning. BR J IND MED 1984 May;41(2):170-8.

*Davies JM. Lung cancer mortality among workers making lead chromate and zinc chromate pigments at three English factories. BR J IND MED 1984 May;41(2):158-69.

Deitch R. Lead in paint. LANCET 1984 Jul 28;2(8396):237-8.

*DeRosa E, Toffolo D, Sigon M, Brighenti F, Gori GP, Bartolucci GB. Evaluation of the current risk of lead poisoning in the ceramics industry. SCAND J WORK ENVIRON HEALTH 1983 Dec;9(6):463-9.

Dessing M, Paulev PE. Blood- and air-lead concentrations during five years of occupational exposure: the effectiveness of an occupational hygiene programme and problems due to welding operations. ANN OCCUP HYG 1983;27(4):367-72.

*Duggan MJ. Contribution of lead in dust to children's blood lead. ENVIRON HEALTH PERSPECT 1983 Apr;50:371-81.

Eisenberg A, Avni A, Acker C, Shahin S, Hamdalla MA, Costin C, Swartz T, Weissenberg E, Grauer F. Stoneground flour as source of lead poisoning [letter]. LANCET 1984 Apr 28;1(8383):972-3.

*Elvestad K, Karlog O, Clausen B. Heavy metals (copper, cadmium, lead, mercury) in mute swans from Denmark. NORD VET MED 1982 Mar;34(3):92-7.

Elwood PC. Blood lead and petrol lead [letter]. BR MED J [Clin Res] 1983 May 7;286(6376):1515.

Elwood PC. Turin isotopic lead experiment [letter]. LANCET 1983 Apr 16;1(8329):869.

Elwood PC, Essex-Cater A, Robb RC. Blood lead levels on islands [letter]. LANCET 1984 Aug 11;2(8398):355.

Elwood PC, Gallacher J. Blood lead levels, 1976-1980 [letter]. N ENGL J MED 1984 Apr 26;310(17):1125-6.

*Elwood PC, Gallacher JE, Phillips KM, Davies BE, Toothill C. Greater contribution to blood lead from water than from air. NATURE 1984 Jul 12-18;310(5973):138-40.

*Elwood PC, Phillips KM, Lowe N, Phillips JK, Toothill C. Hardness of domestic water and blood lead levels. HUM TOXICOL 1983 Oct;2(4):645-8.

Engst R, Konig R, Beckmann G, Lauterbach K. Lead and cadmium contamination of foods and feeds from selected areas of the Erfurt district. 4. Lead in vegetables grown in culture centers of the Erfurt region. NAHRUNG 1983;27(7):633-43.

*Eylenbosch WJ, van Sprundel MP, Clara RR. Lead pollution in Antwerpen, Belgium. ANN ACAD MED SINGAPORE 1984 Apr;13(2):224-30.

*Falahi-Ardakani A. Contamination of environment with heavy metals emitted from automotives. ECOTOXICOL ENVIRON SAFETY 1984 Apr;8(2):152-61.

*Favretto LG. A tentative classification of agricultural foods exposed to roadside lead contamination. Z LEBENSM UNTERS FORSCH 1984 Jun;178(6):450-2.

Fischbein A. Effects of present and past occupational exposures [letter]. NY STATE J MED 1985 Jan;85(1):8-9.

Fischbein A, Leeds M, Solomon S. Lead exposure among iron workers in New York City. A continuing occupational hazard in the 1980s. NY STATE J MED 1984 Sep;84(9):445-8.

Frape DL, Pringle JD. Toxic manifestations in a dairy herd consuming haylage contaminated by lead. VET REC 1984 Jun 23;114(25):615-6.

*Gallacher J, Harris L, Elwood PC. Lead toxicity from water [letter]. NATURE 1983 Sep 22-28;305(5932):280.

*Gallacher JE, Elwood PC, Phillips KM, Davies BE, Ginnever RC, Toothill C, Jones DT. Vegetable consumption and blood lead concentrations. J EPIDEMIOL COMMUNITY HEALTH 1984 Jun;38(2):173-6.

*Gallacher JE, Elwood PC, Phillips KM, Davies BE, Jones DT. Relation between pica and blood lead in areas of differing lead exposure. ARCH DIS CHILD 1984 Jan;59(1):40-4.

*Garrettson LK. Direct and indirect chemical exposure in children. CLIN LAB MED 1984 Sep;4(3):469-73.

Ghafour SY, Khuffash FA, Ibrahim HS, Reavey PC. Congenital lead intoxication with seizures due to prenatal exposure. CLIN PEDIATR (Phila) 1984 May;23(5):282-3.

*Abstracted

*Glickman L, Valciukas JA, Lilis R, Weisman I. Occupational lead exposure. Effects on saccadic eye movements. INT ARCH OCCUP ENVIRON HEALTH 1984;54(2):115-25.

*Glickman L, Valciukas JA, Lilis R, Weisman I. Saccadic eye movements among copper smelter workers. AM J IND MED 1985;7(2):141-53.

Gloag D. A cooler look at lead [editorial]. BR MED J [Clin Res] 1983 May 7;286(6376):1458-9.

*Goldstein RB, Silverberg JS, Martin HF. A multivariate statistical method for the establishment of maximum allowable exposure to toxic materials in the workplace. AM J IND MED 1984;6(6):459-73.

*Grandjean P, Wulf HC, Niebuhr E. Sister chromatid exchange in response to variations in occupational lead exposure. ENVIRON RES 1983 Oct;32(1):199-204.

Gupta BN, Mathur AK. Toxicity of heavy metals (a review). INDIAN J MED SCI 1983 Dec;37(12):236-40.

*Haavikko K, Anttila A, Helle A, Vuori E. Lead concentrations of enamel and dentine of deciduous teeth of children from two Finnish towns. ARCH ENVIRON HEALTH 1984 Mar-Apr;39(2):78-84.

Handson PD. Lead and arsenic levels in wines produced from vineyards where lead arsenate sprays are used for caterpillar control. J SCI FOOD AGRIC 1984 Feb;35(2):215-8.

*Hansen JC, Kromann N, Wulf HC, Alboge K. Human exposure to heavy metals in East Greenland. II. Lead. SCI TOTAL ENVIRON 1983 Feb;26(3):245-54.

*Harrison RM, Williams CR. Physico-chemical characterization of atmospheric trace metal emissions from a primary zinc-lead smelter. SCI TOTAL ENVIRON 1983 Nov;31(2):129-40.

*Haschke F, Steffan I, Schilling R, Schuster E, Salzer HP. Lead content of water and of reconstituted infant formula in Vienna. MINER ELECTROLYTE METAB 1985;11(1):45-51.

Healy MA, Aslam M. Identification of lead in Asian cosmetics—a test for use by health visitors. PUBLIC HEALTH 1984 Nov;98(6):361-6.

Healy MA, Aslam M, Bamgboye OA. Traditional medicine and lead-containing preparations in Nigeria. PUBLIC HEALTH 1984 Jan;98(1):26-32.

*Hershko C, Abrahamov A, Moreb J, Hersh M, Shiffman R, Shahin A, Richter ED, Konijn AM, Weissenberg E, Graver F, et al. Lead poisoning in a West Bank Arab Village. ARCH INTERN MED 1984 Oct;144(10):1969-73.

*Hinton D, Cresswell BC, Janus ED, Malpress WA. Industrial lead exposure: a review of blood lead levels in South Island industries, 1974-83. NZ MED J 1984 Nov 14;97(767):769-73.

Hoffmann M, Hagberg S, Karlsson A, Nilsson R, Ranstam J, Hogstedt B. Inorganic lead exposure does not effect lymphocyte micronuclei in car radiator repair workers. HEREDITAS 1984;101(2):223-6.

*Huel G, Everson RB, Menger I. Increased hair cadmium in newborns of women occupationally exposed to heavy metals. ENVIRON RES 1984 Oct;35(1):115-21.

*Jarvinen V, Anttila A, Lappalainen R, Rytomaa I. Lead content of deciduous molar enamel in Finland, as measured by proton-induced X-ray emission. SCAND J WORK ENVIRON HEALTH 1984 Apr;10(2):103-7.

Johnson L, Barlow PJ, Barratt RS. Lead in paint—brushed aside? J R SOC HEALTH 1984 Apr;104(2):64-7.

Johnson L, Barlow PJ, Barratt RS. Paint lead levels in a restricted environment. J R SOC HEALTH 1984 Jun;104(3):96-8.

Jones W, Gamble J. Epidemiological-environmental study of lead acid battery workers. I. Environmental study of five lead acid battery plants. ENVIRON RES 1984 Oct;35(1):1-10.

Kaphalia BS, Chandra H, Bhargava SK, Seth TD, Gupta BN. Lead in drinking water. INDIAN J PUBLIC HEALTH 1983 Apr-Jun;27(2):64-9.

*Karai I, Lee SI, Horiguchi S, Fukumoto K, Matsumura S, Takise S. Combined effects of lead and EDTA on Na^+,K^+-ATPase activity of erythrocyte membranes. J TOXICOL ENVIRON HEALTH 1983 Oct-Dec;12(4-6):721-30.

*Katagiri Y, Toriumi H, Kawai M. Lead exposure among 3-year-old children and their mothers living in a pottery-producing area. INT ARCH OCCUP ENVIRON HEALTH 1983;52(3):223-9.

*Khandekar RN, Mishra UC, Vohra KG. Environmental lead exposure of an urban Indian population. SCI TOTAL ENVIRON 1984 Dec;40:269-78.

*Kovar IZ, Strehlow CD, Richmond J, Thompson MG. Perinatal lead and cadmium burden in a British urban population. ARCH DIS CHILD 1984 Jan;59(1):36-9.

Kurono T. Lead content in food in Japan in the early 1980's with the estimation of its daily intake. OSAKA CITY MED J 1983;29(1):15-41.

Lacy R, Winternitz WW. Moonshine consumption in West Alabama. ALA J MED SCI 1984 Oct;21(4):364-5.

*Lauwerys R, Roels H, Buchet JP, Bernard AA, Verhoeven L, Konings J. The influence of orally-administered vitamin C or zinc on the absorption of and the biological response to lead. J OCCUP MED 1983 Sep;25(9):668-78.

Lenihan J. Hazards from lead in the environment. PRACTITIONER 1983 Sep;227(1383):1373-80.

*Abstracted

Levitt C, Godes J, Eberhardt M, Ing R, Simpson JM. Sources of lead poisoning [letter]. JAMA 1984 Dec 14;252(22):3127-8.

*Lilis R, Valciukas JA, Weber JP, Fischbein A, Nicholson WJ, Campbell C, Malkin J, Selikoff IJ. Distribution of blood lead, blood cadmium, urinary cadmium, and urinary arsenic levels in employees of a copper smelter. ENVIRON RES 1984 Feb;33(1):76-95.

Lim Heng Huat, Abu Bakar CM. Occupational exposure to inorganic lead in Malaysian battery-manufacturing factories. MED J MALAYSIA 1983 Sep;38(3):212-6.

*Loureiro S, Spinola AG, Carvalho FM, Barreto ML. Lead poisoning and hookworm infection as multiple factors in anaemia. TRANS R SOC TROP MED HYG 1983;77(3):321-2.

Lubin AH, Signs SA, Caffo A. Tapwater lead in homes of children with undue body lead burden. OHIO STATE MED J 1984 Jul;80(7):547-51.

Lurakis MF, Pitone JM. Occupational lead exposure, acute intoxication, and chronic nephropathy: report of a case and review of the literature. J AM OSTEOPATH ASSOC 1984 Jan;83(5):361-6.

*Mahaffey KR. Sources of lead in the urban environment [editorial]. AM J PUBLIC HEALTH 1983 Dec;73(12):1357-8.

*Manor E, Freundlich E. Lead poisoning from ceramics in the Arab population. ARCH TOXICOL [Suppl] 1983;6:275-8.

Marletta GP, Favretto LG. Preliminary investigation on the balance of lead and cadmium content in milk and its by-products. Z LEBENSM UNTERS FORSCH 1983;176(1):32-5.

Marshall E. Senate considers lead gasoline ban [news]. SCIENCE 1984 Jul 6;225(4657):34-5.

*Mart L, Rutzel H, Klahre P, Sipos L, Platzek U, Valenta P, Nurnberg HW. Comparative studies on the distribution of heavy metals in the oceans and coastal waters. SCI TOTAL ENVIRON 1982 Dec;26(1):1-17.

*McIntosh MJ, Moore MR, Goldberg A, Fell GS, Cunningham C, Halls DJ. Studies of lead and cadmium exposure in Glasgow, U.K. ECOL DIS 1982;1(2-3):177-84.

*Meyer BR, Fischbein A, Rosenman K, Lerman Y, Drayer DE, Reidenberg MM. Increased urinary enzyme excretion in workers exposed to nephrotoxic chemicals. AM J MED 1984 Jun;76(6):989-98.

*Mielke HW, Anderson JC, Berry KJ, Mielke PW, Chaney RL, Leech M. Lead concentrations in inner-city soils as a factor in the child lead problem. AM J PUBLIC HEALTH 1983 Dec;73(12):1366-9.

*Mielke HW, Blake B, Burroughs S, Hassinger N. Urban lead levels in Minneapolis: the case of the Hmong children. ENVIRON RES 1984 Jun;34(1):64-76.

Miller CH. The silent risk of rifle shooting. OCCUP HEALTH (Lond) 1984 Aug;36(8):365.

*Molina-Ballesteros G, Zuniga-Charles MA, Cardenas Ortega A, Solis-Camara R P, Solis-Camara V P. Lead concentrations in the blood of children from pottery-making families exposed to lead salts in a Mexican village. BULL PAN AM HEALTH ORGAN 1983;17(1):35-41.

Myers WR, Peach MJ 3d, Allender J. Workplace protection factor measurements on powered air-purifying respirators at a secondary lead smelter—test protocol. AM IND HYG ASSOC J 1984 Apr;45(4):236-41.

Needleman HL. Childhood lead poisoning [letter]. AM J DIS CHILD 1983 Oct;137(10):1025.

*Nevissi AE. Measurement of ^{210}Pb atmospheric flux in the Pacific Northwest. HEALTH PHYS 1985 Feb;48(2):169-74.

*Nriagu JO. Occupational exposure to lead in ancient times. SCI TOTAL ENVIRON 1983 Nov;31(2):105-16.

Okubo T, Omae K, Sakurai H, Sugita M, Tsuchiya K. The relationship of airborne lead to blood lead in school children. SANGYO IKA DAIGAKU ZASSHI 1983 Mar 20;5 Suppl:137-44.

Palmer HE, Heid KR, Moore RH. Lead-210 in uranium mine and mill workers. HEALTH PHYS 1984 Oct;47(4):632-4.

Perrelli G, Capellaro E, Pira E, Maina G, Vergnano P. Further cases of lead poisoning from wine. AM J IND MED 1984;5(5):377-81.

Poma PA. A dangerous folk therapy. J NATL MED ASSOC 1984 Apr;76(4):387-9.

*Price J, Baddeley H, Kenardy JA, Thomas BJ, Thomas BW. In vivo X-ray fluorescence estimation of bone lead concentrations in Queensland adults. BR J RADIOL 1984 Jan;57(673):29-33.

*Prpic-Majic D, Meczner J, Telisman S, Kersanc A. Biological monitoring of lead effects in a smelter community before and after emission control. SCI TOTAL ENVIRON 1984 Jan 27;32(3):277-88.

Que Hee SS, Lawrence P. Inhalation exposure of lead in brass foundry workers: the evaluation of the effectiveness of a powered air-purifying respirator and engineering controls. AM IND HYG ASSOC J 1983 Oct;44(10):746-51.

*Rabinowitz M, Leviton A, Bellinger D. Home refinishing, lead paint, and infant blood lead levels. AM J PUBLIC HEALTH 1985 Apr;75(4):403-4.

*Rabinowitz M, Needleman H, Burley M, Finch H, Rees J. Lead in umbilical blood, indoor air, tap water, and gasoline in Boston. ARCH ENVIRON HEALTH 1984 Jul-Aug;39(4):299-301.

*Abstracted

*Rabjerg L, Jennum PJ, Morck HI. White lead exposure among Danish police officers employed in fingerprint detection. SCAND J WORK ENVIRON HEALTH 1983 Dec;9(6):511-3.

*Redetzki HM, Kearney TE, Ratard RC. Evaluation and cleanup of a lead monoxide spill in Greenwood, Louisiana. VET HUM TOXICOL 1984;26 Suppl 2:36-7.

Refowitz RM. Thyroid function and lead: no clear relationship. J OCCUP MED 1984 Aug;26(8):579-83.

Reynolds PP, Knapp MJ, Baraf HS, Holmes EW. Moonshine and lead. Relationship to the pathogenesis of hyperuricemia in gout. ARTHRITIS RHEUM 1983 Sep;26(9):1057-64.

*Rockway SW, Weber CW, Lei KY, Kemberling SR. Lead concentrations of milk, blood, and hair in lactating women. INT ARCH OCCUP ENVIRON HEALTH 1984;53(3):181-7.

Rowan CA, Connolly WM, Brown HS. Evaluating the use of occupational standards for controlling toxic air pollutants. J ENVIRON SCI HEALTH [B] 1984 Oct;19(7):611-48.

*Ryu JE, Ziegler EE, Nelson SE, Fomon SJ. Dietary intake of lead and blood lead concentration in early infancy. AM J DIS CHILD 1983 Sep;137(9):886-91.

*Saric M. Reproduction and exposure to lead. ANN ACAD MED SINGAPORE 1984 Apr;13(2 Suppl):383-8.

*Sato K, Fujita H, Inui S, Ikeda M. Changes in urinary δ-aminolevulinic acid at low lead exposure level with special reference to production activity. INT ARCH OCCUP ENVIRON HEALTH 1983;52(1):25-32.

*Scott D. Lead intoxication. Controlling lead exposure in removal of old paint. POSTGRAD MED 1983 Sep;74(3):92-3.

Seppalainen AM, Hernberg S. A follow-up study of nerve conduction velocities in lead exposed workers. NEUROBEHAV TOXICOL TERATOL 1982 Nov-Dec;4(6):721-3.

*Sherlock JC, Ashby D, Delves HT, Forbes GI, Moore MR, Patterson WJ, Pocock SJ, Quinn MJ, Richards WN, Wilson TS. Reduction in exposure to lead from drinking water and its effect on blood lead concentrations. HUM TOXICOL 1984 Oct;3(5):383-92.

*Sherlock JC, Smart GA, Read JI, Brooke PJ, Forbes G, Patterson W, Richards W, Moore M, Wilson T. Intakes of copper, zinc, cadmium, tin, iron, nickel and arsenic in a population exposed to lead from water. SCI TOTAL ENVIRON 1983 Sep;30:255-60.

Sherlock JC, Smart GA, Walters B, Evans WH, McWeeny DJ, Cassidy W. Dietary surveys on a population at Shipham, Somerset, United Kingdom. SCI TOTAL ENVIRON 1983 Jul;29(1-2):121-42.

Shore SH, Morgan G, Cross PJ. Lead poisoning in cattle and geese [letter]. VET REC 1984 Feb 4;114(5):126-7.

*Shukla GS, Singhal RL. The present status of biological effects of toxic metals in the environment: lead, cadmium, and manganese. CAN J PHYSIOL PHARMACOL 1984 Aug;62(8):1015-31.

Skerfving S, Ahlgren L, Christoffersson JO, Haeger-Aronsen B, Mattsson S, Schutz A. Metabolism of inorganic lead in occupationally exposed humans. ARH HIG RADA TOKSIKOL 1983 Dec;34(4):341-50.

Smith-Briggs JL, Bradley EJ. Measurement of natural radionuclides in U.K. diet. SCI TOTAL ENVIRON 1984 May 1;35(3):431-40.

*Sparrow D, Sharrett AR, Garvey AJ, Craun GF, Silbert JE. Trace metals in drinking water: lack of influence on blood pressure. J CHRONIC DIS 1984;37(1):59-65.

Stephens R, Russell Jones R. Blood lead on a traffic-free island [letter]. LANCET 1984 Oct 27;2(8409):976.

Taylor A, Majumdar G, Delves HT. Probable self-administration of lead [letter]. LANCET 1985 Mar 2;1(8427):513.

Taylor JR. Neurotoxicity of certain environmental substances. CLIN LAB MED 1984 Sep;4(3):489-97.

Taymaz K, Yigit V, Ozbal H, Ceritoglu A, Muftugil N. Heavy metal concentrations in water, sediment and fish from Izmit Bay, Turkey. INT J ENVIRON ANAL CHEM 1984;16(4):253-65.

Thornton I, Abrahams P. Soil ingestion—a major pathway of heavy metals into livestock grazing contaminated land. SCI TOTAL ENVIRON 1983 Jun;28:287-94.

*Tollerud DJ, Weiss ST, Elting E, Speizer FE, Ferris B. The health effects of automobile exhaust. VI. Relationship of respiratory symptoms and pulmonary function in tunnel and turnpike workers. ARCH ENVIRON HEALTH 1983 Nov-Dec;38(6):334-40.

*Triebig G, Weltle D, Valentin H. Investigations on neurotoxicity of chemical substances at the workplace. V. Determination of the motor and sensory nerve conduction velocity in persons occupationally exposed to lead. INT ARCH OCCUP ENVIRON HEALTH 1984;53(3):189-203.

*Tsuchiya H, Mitani K, Kodama K, Nakata T. Placental transfer of heavy metals in normal pregnant Japanese women. ARCH ENVIRON HEALTH 1984 Jan-Feb;39(1):11-7.

*van Wyk CW, Grobler SR. Lead levels in deciduous teeth of children from selected urban areas in the Cape Peninsula. S AFR MED J 1983 Apr 9;63(15):559-62.

Ventura A, Senin U, Mannarino E. Iron pathology in the elderly. BIBL NUTR DIETA 1983;(33):113-20.

*Abstracted

*Wang YL. Industrial lead poisoning in China over the past 33 years. ECOTOXICOL ENVIRON SAFETY 1984 Dec;8(6):526-30.

*Wijn M, Duives P, Herber R, Brunekreef B. Lead uptake from vegetables grown along highways. INT ARCH OCCUP ENVIRON HEALTH 1983;52(3):263-70.

*Williams MK. Biological tests of lead absorption following a brief massive exposure. J OCCUP MED 1984 Jul;26(7):532-3.

*Wolff MS. Occupationally derived chemicals in breast milk. PROG CLIN BIOL RES 1983;117:259-81.

Wolnik KA, Fricke FL, Capar SG, Braude GL, Meyer MW, Satzger RD, Bonnin E. Elements in major raw agricultural crops in the United States. 1. Cadmium and lead in lettuce, peanuts, potatoes, soybeans, sweet corn, and wheat. J AGRIC FOOD CHEM 1983 Nov-Dec;31(6):1240-4.

*Yaffe Y, Flessel CP, Wesolowski JJ, del Rosario A, Guirguis GN, Matias V, Gramlich JW, Kelly WR, Degarmo TE, Coleman GC. Identification of lead sources in California children using the stable isotope ratio technique. ARCH ENVIRON HEALTH 1983 Jul-Aug;38(4):237-45.

Yoshida K, Sakurai H. Anemic changes in lead-exposed workers after onset of exposure. KEIO J MED 1984 Apr;33(1):29-38.

*Zimmermann-Tansella C, Campara P, D'Andrea F, Savonitto C, Tansella M. Psychological and physical complaints of subjects with low exposure to lead. HUM TOXICOL 1983 Oct;2(4):615-23.

*Abstracted

DIAGNOSIS AND SCREENING

The "Lead-Induced Colic" Syndrome in Lead Intoxication

Y. Janin, C. Couinaud, A. Stone, and L. Wise. SURG ANNU 1985;17:287-307.

Authors' abstract: Lead has a multiplicity of biologic effects. The universal occurrence of lead accounts for the continuous appearance of new instances of human lead poisoning. The most common and one of the earliest manifestations of lead intoxication in the adult is so-called lead-induced colic, which is a syndrome with a multiplicity of clinical patterns and at least three possible different pathogenic mechanisms. It may be caused by changes in the visceral smooth muscle tone secondary to the action of lead on the visceral autonomic nervous system, lead-induced alterations in sodium transport in the small-intestinal mucosa, and lead-induced interstitial pancreatitis. It should be considered in the differential diagnosis of abdominal pain of obscure etiology and whenever a disparity is observed between the symptoms and the abdominal findings in a patient with abdominal pain, especially in the presence of a history of occupational exposure to lead.

Basophilic Stippling of Red Blood Cells: A Nonspecific Finding of Multiple Etiology

B.D. Cheson, W.N. Rom, and R.C. Webber. AM J IND MED 1984;5(4):327-34.

Authors' abstract: Basophilic stippling of red blood cells (BSC) has been noted in lead intoxication since 1899 and has been considered a classic laboratory sign of lead poisoning since that time. BSC's are inclusions of aggregated ribosomes found only in the red blood cells and may be confused with siderotic (iron) granules, Heinz Bodies, or even reticulocytes. BSC's are an inconstant finding in lead intoxication. In a review of peripheral blood smears from 1,000 consecutive internal medicine patients, we found BSC in 27%. These occurred in a variety of malignant, rheumatologic, hematologic, cardiovascular, and other diseases, frequently with an associated anemia. BSC may even be found in a small percentage of normal people; thus, it must be emphasized that BSC is a nonspecific finding. Furthermore, BSC has been replaced by blood lead (since the 1940's) and zinc protoporphyrin (since the 1970's) levels for biologic monitoring of lead-exposed workers.

Organic Affective Illness Associated with Lead Intoxication

R.S. Schottenfeld and M.R. Cullen. AM J PSYCHIATRY 1984 Nov;141(11):1423-6.

Authors' abstract: Psychiatrists treating patients with depression or nonspecific somatic complaints seldom think of lead intoxication as a possible cause. Because occupational exposure to lead is so common, these disturbances may often be associated with lead intoxication. To facilitate earlier clinical recognition and proper treatment among the many individuals at risk, the authors describe four cases of organic affective disturbance associated with lead intoxication, review the neuropsychiatric disturbances that have been reported with chronic exposure to lead, and report the results of their experience evaluating the psychiatric aspects of lead intoxication among individuals exposed in their work.

Lead-Induced Convulsions in Young Infants — A Case History and the Role of GABA and Sodium Valproate in the Pathogenesis and Treatment

M.A. Healy, M. Aslam, P.G. Harrison, and N.P. Fernando. J CLIN HOSP PHARM 1984 Sep;9(3):199-207.

Authors' abstract: A detailed case history of lead poisoning in a young infant is presented. Attention is directed towards the nature of the induced convulsions observed in such cases and the possible role of the GABAergic neuroinhibitory system. In vitro data demonstrating direct lead-GABA interaction is presented, and sodium valproate, an effective anticonvulsant that affects GABA function, is shown to be an appropriate agent for medication in lead-induced convulsions. The hypothesis is presented that lead interacts with GABA, which thereby reduces the neuroinhibition, and that this may be counteracted by the action of sodium valproate.

Lead Poisoning as a Toxogenetic Disease

M. Doss, H. Baumann, M. Lorrek, F. Laubenthal, and J. Schneider. KLIN WOCHENSCHR 1984 May 2;62(9):430-1.

Authors' abstract: In two nonrelated patients suffering from acute lead intoxication a persistent decrease in red

cell δ-aminolevulinic acid dehydratase (synonym: porphobilinogen synthase) activity of 30%-60% of controls was noted after treatment and normalization of lead levels and heme precursors in urine and blood. An inherited enzyme deficiency was suggested and confirmed by a subnormal activity in the mothers of both patients. These four persons are considered as heterozygotes with an increased sensitivity to lead exposure.

Lead Poisoning in Inherited δ-Aminolevulinic Acid Dehydratase Deficiency

M. Doss, F. Laubenthal, and M. Stoeppler. INT ARCH OCCUP ENVIRON HEALTH 1984;54(1):55-63.

Authors' abstract: δ-Aminolevulinic acid dehydratase [(ALA-D), respectively porphobilinogen synthase, EC 4.2.1.24)] activity can be lowered by toxic, metabolic, and hereditary factors. A 30-year-old painter was suffering from lead poisoning with an acute abdominal-neurologic syndrome and anemia. Blood lead was measured at 414 μg/l. Urinary ALA and coproporphyrin excretion as well as erythrocyte protoporphyrin had increased extremely, whereas ALA-D activity in erythrocytes had decreased extremely to 8% of controls. Excretion parameters, protoporphyrin, hemoglobin, and lead returned to normal after treatment, but 4 years later ALA-D activity still remained diminished (30% of controls). An inherited enzyme deficiency was assumed and found in the mother, analogous to the subnormal ALA-D activity in heterozygotes of four other families. The inherited enzyme deficiency sensitized the patient to lead exposure and intoxication, which is a toxogenetic disease in this case.

An Association Between Increased Porphyrin Precursors and Onset of Abdominal Symptoms in Lead Poisoning

Y. Okamoto and M. Kawai. TOXICOL LETT 1984 May;21(2):219-23.

Authors' abstract: To examine a potential role of porphyrinopathy induced by lead (Pb) exposure in the pathogenesis of constipation in Pb poisoning, we subjected a Pb-intoxicated worker to the serial determinations for various biochemical indicators of Pb exposure in relation to the onset of constipation. The results have shown that the onset of constipation parallels a rapid rise in either urinary δ-aminolevulinic acid (ALA) or coproporphyrin (CP), or both. The present evidence is not yet conclusive about the involvement of porphyrinopathic mechanism in the development of constipation in Pb intoxication.

Immunological and Enzymatic Studies of Erythrocytic δ-Aminolevulinate Dehydratase. Comparison of Results Obtained in Normal and Lead-Exposed Subjects

C. Boudene, N. Despaux-Pages, E. Comoy, and C. Bohuon. INT ARCH OCCUP ENVIRON HEALTH 1984;55(1):87-96.

Authors' abstract: The δ-aminolevulinate dehydratase (ALAD) quantitative assay on a centrifugal fast analyzer showed that subjects whose blood-lead level varies between 30 and 75 μg/100 ml (1.5 to 3.75 μM/l) react to blood intoxication by synthesizing de novo an amount of enzyme correlating to blood-lead levels. At higher concentrations, the reactional synthesis occurs very rarely. These results suggest that enzyme is constitutive, but also inductible as soon as its substrate accumulates; this last ability may disappear at high blood-lead levels.

Lead Poisoning: Hair Analysis Shows the Calendar of Events

P. Grandjean. HUM TOXICOL 1984 Jun;3(3):223-8.

Author's abstract: A woman was given frequent oral doses of lead nitrate over an extended time period. Diagnosis was finally made about 6 months after the first symptoms appeared. Analysis of hair taken at two different times was used as evidence in court. The hair lead concentrations exhibited rapid changes and normalized shortly after chelation treatment had been instituted. This finding suggests that the hair lead level may reflect a current absorption level rather than the lead content of whole blood, which, in this case, changed much more slowly. Despite the extremely high blood lead levels and the severe clinical lead poisoning, lead concentrations in hair were relatively low in comparison to the concentrations found in hair of workers exposed to high levels of airborne lead. This observation suggests that a large proportion of the lead content of hair from individuals with respiratory lead exposure may be exogenous.

A Fatal Case of Lead Poisoning Due to a Retained Bullet

V.J. DiMaio, S.M. DiMaio, J.C. Garriott, and P. Simpson. AM J FORENSIC MED PATHOL 1983 Jun;4(2):165-9.

Authors' abstract: Lead poisoning from a retained bullet or missile is rare and is usually dependent on the location of the missile in a bone or immediately adjacent to a joint. A review of the literature revealed only 14 cases in which there was adequate laboratory documentation of plumbism caused by a retained bullet or missile. Only one of these previously reported cases resulted in death. We report a second death due to lead poisoning from a

retained bullet with elevated blood lead levels documented by toxicologic analysis.

Lead Poisoning from Hair Spray Ingestion

F.O. Raasch, J.H. Rosenberg, and J.L. Abraham. AM J FORENSIC MED PATHOL 1983 Jun;4(2):159-64.

Authors' abstract: A 37-year-old alcoholic woman was poisoned by lead from drinking hair spray mixed with water. Laboratory and pathologic findings showed changes due to lead poisoning. Further analysis by Scanning Electron Microscopy (SEM) and Energy Dispersive X-Ray Analysis (EDXA) confirmed the presence of lead in both the tissues and the hair spray. The significance of these findings is discussed.

Potential Toxicity Due To Dolomite and Bonemeal

H.J. Roberts. SOUTH MED J 1983 May;76(5):556-9.

Author's abstract: Large amounts of dolomite and bonemeal are being consumed, especially by nutrition-conscious persons. The mineral content of commercial samples has been analyzed by different laboratories, and significant amounts of lead, arsenic, mercury, and other potentially toxic metals, which also exist in conventional vitamin-mineral and calcium supplements, were detected. Physicians must consider the possibility of unrecognized self-poisoning from the consumption of such substances, especially in the context of unexplained neurologic, gastrointestinal, cutaneous, and hematologic disorders. The use of dolomite and bonemeal by pregnant women, children with suspected milk allergy, and elderly persons requires careful evaluation.

Trace Elements and Blood Pressure

P. Saltman. ANN INTERN MED 1983 May;98(5 Pt 2):823-7.

Author's abstract: Essential trace elements such as zinc, iron, and copper participate in various enzyme reactions directly related to the regulation of blood pressure and indirectly related to generation of oxidative metabolic energy, alterations in blood lipid levels, and alterations in taste acuity. The toxicological action of several heavy metal ions, including cadmium, lead, mercury, and thallium, can cause hypertension by affecting hormone metabolism, vasoconstriction, and renal tubular function. We conclude, however, that neither deficiencies of essential elements nor the presence of toxic heavy metals are primary causes of hypertension in our population.

Blood Lead Concentration, Blood Pressure, and Renal Function

S.J. Pocock, A.G. Shaper, D. Ashby, T. Delves, and T.P. Whitehead. BR MED J [Clin Res] 1984 Oct 6;289(6449):872-4.

Authors' abstract: Blood lead concentrations were related to blood pressure and indicators of renal function in a clinical survey of 7,735 middle-aged men from 24 British towns. There was no overall evidence that blood lead concentrations were associated with systolic or diastolic blood pressure ($r = +0.03$ and $+0.01$, respectively). In the 74 men with a blood lead concentration of 1.8 μmol/l (37.3 μg/100 ml) or more there was some suggestion of increased hypertension, but this did not reach significance. Blood lead concentration did not have any relation with serum creatinine concentration. Moderate increases in blood lead concentration were associated with small increases in mean serum urate concentration and small decreases in mean serum urea concentration; these associations were both reduced when alcohol consumption was taken into account. There is no indication that exposure to lead at concentrations commonly encountered in British men is responsible for impaired renal function or increased blood pressure.

The Safety of the EDTA Lead-Mobilization Test

R.P. Wedeen, V. Batuman, and E. Landy. ENVIRON RES 1983 Feb;30(1):58-62.

Authors' abstract: The effect of the $CaNa_2EDTA$ lead-mobilization test on renal function was determined in 122 patients. Three days, 7 days, and 4 weeks after the test, the mean serum creatinine was not significantly increased. These data indicate that the EDTA test is not nephrotoxic even in patients with preexisting renal disease.

Occult Lead Intoxication in Patients with Gout and Kidney Disease

L.F. Wright, R.P. Saylor, and F.A. Cecere. J RHEUMATOL 1984 Aug;11(4):517-20.

Authors' abstract: Ten patients with gout, hypertension, and mild to moderate renal insufficiency were studied for possible lead nephropathy by measuring stimulated urinary lead excretion. Seven had a history of lead exposure, five from illegal alcohol and two from industrial sources. Occult lead was assessed by 24-h urine collection measurements over a 72-h period after intramuscular administration of calcium disodium EDTA. Two patients with a history of lead exposure excreted 707 and 687 μg Pb/72 h, respectively, and a third excreted 506 μg Pb/72 h. The remainder had a normal response, with mean urinary lead excretion of 251

± 42 μg Pb/72 h. Since we were unable to demonstrate that lead was important to the pathogenesis of the renal failure in seven patients despite a positive history of lead exposure in two, we suggest that factors other than lead may be the cause of renal failure in most patients with gout and renal disease.

Contribution of Lead to Hypertension with Renal Impairment

V. Batuman, E. Landy, J.K. Maesaka, and R.P. Wedeen. N ENGL J MED 1983 Jul 7;309(1):17-21.

Authors' abstract: Hypertension of unknown cause is generally termed "essential." Because hypertension has long been considered a possible complication of lead poisoning and the EDTA lead-mobilization test has proved to be a sensitive indicator of excessive body stores of lead, we used this test to evaluate cumulative past lead absorption in 48 men diagnosed as having essential hypertension. Patients who had hypertension with reduced renal function (i.e., serum creatinine level > 1.5 mg per deciliter [133 μmol per liter]) had significantly larger amounts of mobilizable lead than did patients who had hypertension without renal impairment. The increase in mobilizable lead was not due to the renal disease itself, since 22 control patients without a history of essential hypertension but with comparable renal impairment from known causes excreted significantly less lead chelate during the 3-day test. These data suggest that lead may have an etiologic role in the renal disease of some patients usually designated as having "essential" hypertension.

Chronic Renal Failure with Gout: A Marker of Chronic Lead Poisoning

P.W. Craswell, J. Price, P.D. Boyle, V.J. Heazlewood, H. Baddeley, H.M. Lloyd, B.J. Thomas, and B.W. Thomas. KIDNEY INT 1984 Sep;26(3):319-23.

Authors' abstract: EDTA (calcium disodium edetate) lead mobilization and x-ray fluorescence (XRF) finger bone lead tests were done in 42 patients with chronic renal failure and without persisting lead intoxication. Nineteen of 23 patients with gout and 8 of 19 without gout had positive EDTA lead mobilization tests. Those patients with gout excreted significantly more excess lead chelate than those without gout. In the gout group, 17 patients denied any childhood or industrial exposure to lead. They had a greater number of positive tests and excreted significantly more excess lead chelate than 14 patients with neither gout nor lead exposure. These results confirm that gout in the presence of chronic renal failure is a useful marker of chronic lead poisoning. Of 27 patients with positive lead mobilization tests, only 13 had elevated XRF finger bone lead concentrations (sensitivity 48%). Three of 15 patients with negative lead mobilization tests had elevated XRF finger bone lead concentrations (specificity 80%). Although the XRF finger bone lead test is a convenient noninvasive addition to the diagnostic evaluation of patients with chronic renal failure and gout, its application is limited because of the lack of sensitivity of the method.

Lead in Finger-Bone Analysed in Vivo in Active and Retired Lead Workers

J.O. Christoffersson, A. Schutz, L. Ahlgren, B. Haeger-Aronsen, S. Mattsson, and S. Skerfving. AM J IND MED 1984;6(6):447-57.

Authors' abstract: In 75 active lead workers the median lead level in finger-bone (bone-Pb), as determined in vivo by an X-ray fluorescence method, was 43 μg/g (range < 20-122). In 32 retired workers the median level was even higher, 59 μg/g (range < 20-135), which indicates a slow turnover rate of lead in finger-bone. This was confirmed in 18 of the "active" workers in whom bone-Pb was studied in connection with an exposure-free period. In spite of a significant decrease in blood-lead levels (B-Pb), no systematic change of bone-Pb occurred. There was an increase of bone-Pb with time of employment, but with a large interindividual variation. No association was found between bone-Pb and present B-Pb in the active lead workers. However, in the retired ones, B-Pb rose with increasing bone-Pb. The bone-lead pool thus causes an "internal" lead exposure.

Feasibility of Noninvasive Analysis of Lead in the Human Tibia by Soft X-Ray Fluorescence

L. Wielopolski, J.F. Rosen, D.N. Slatkin, D. Vartsky, K.J. Ellis, and S.H. Cohn. MED PHYS 1983 Mar-Apr;10(2):248-51.

Authors' abstract: A postmortem study was conducted to assess the feasibility of measuring bone lead concentrations noninvasively in vivo. Characteristic L x rays were induced with an external source of ^{125}I in the superficial tibial cortex of the intact legs of six adults who had no history of occupational exposure to lead. Tibial lead concentrations in the same bones subsequently determined by flameless atomic absorption spectroscopy varied from 15 to 35 μg Pb/g wet weight. The upper limit for the modern normal range of lead in the bone is about 25 mg Pb/g wet tissue. The linear correlation coefficient (r) between the measurements made with x-ray fluorescence and lead concentration by absorption spectroscopy was 0.90. Radiation doses of 10 mGy (1 rad) to 1 cm^2 of skin, with associated doses to the marrow of adjacent bone of about 0.6 mGy (60 mrad), yielded net lead fluorescence signals ranging from one to seven times the standard deviation of background.

Subjective Symptoms in Workers with Low-Level Exposure to Lead

A. Fischbein, J.C. Thornton, L. Sarkozi, S. Kon, and S. Levin. J APPL TOXICOL 1982 Dec;2(6):289-93.

Authors' abstract: In an attempt to identify health effects associated with low-level lead exposure, we examined 45 cable-manufacturing workers in a cross-sectional study. Thirteen workers were in direct contact with lead-containing stabilizers, and 31 were only indirectly exposed. The directly exposed had a higher prevalence of reported neurological and gastrointestinal symptoms than those with low or insignificant lead exposure. None of the directly exposed had blood lead levels exceeding 60 μg per 100 ml. The clinical symptoms correlated with blood lead and zinc protoporphyrin. However, when the data were subjected to hierarchical log-linear modeling, a partial association was found between zinc protoporphyrin and symptoms, but not between blood lead and symptoms. The data suggest that nonspecific neurological and gastrointestinal symptoms may occur at relatively low blood lead and zinc protoporphyrin levels and that measurement of zinc protoporphyrin and exploration of clinical symptoms are valuable components in lead screening programs.

Subjective Symptoms After Long Term Lead Exposure in Secondary Lead Smelting Workers

H. Kirkby, C.J. Nielsen, V.K. Nielsen, and F. Gyntelberg. BR J IND MED 1983 Aug;40(3):314-7.

Authors' abstract: The prevalence of lead-induced subjective symptoms was evaluated by a standardized questionnaire in a group of 96 workers employed between 9 and 45 years in a secondary lead smelting works. A control group of 96 non-lead-exposed subjects, matched for age and sex, were chosen from the Glostrup population study. Blood lead concentrations were in excess of 60 μg/100 ml in about 30% of the lead workers. Zinc protoporphyrin levels were found to be higher than 500 μmol/Hb in nearly 18% of the lead workers. The prevalence of fatigue, headache, sleep disturbance, and digestive symptoms (constipation and colic) were not higher in the lead-exposed group. The body weight showed no significant difference in the two groups. Nervousness was four times more frequent in the control group. The results indicate that subjective symptoms are useless as indicators of incipient lead poisoning.

Neurophysiological Studies on Workers Exposed to Lead

J. Jeyaratnam, G. Devathasan, C.N. Ong, W.O. Phoon, and P.K. Wong. BR J IND MED 1985 Mar;42(3):173-7.

Authors' abstract: Nerve conduction and somatosensory evoked potential studies were undertaken on 46 workers exposed to a combination of organic and inorganic lead. In addition, electroencephalograms (EEG's) were carried out on 20 of the workers; the results were compared with those obtained for workers not exposed to lead. The workers exposed to lead had a mean blood lead concentration of 2.35 μmol/l (48.7 μg/100 ml), whereas the concentration for workers not exposed to lead was 0.76 μmol/l (15.8 μg/100 ml). The mean maximum motor conduction velocities of the median and the posterior tibial nerves were significantly lower in the workers exposed to lead than in the controls. Similarly, the distal latency for these two nerves was significantly prolonged for the workers exposed to lead. No significant differences for the two groups of workers were seen in the nerve conduction and distal latency measurements of the median (sensory) and the sural nerves. The EEG studies of the 20 workers exposed to lead showed no abnormalities. The somatosensory evoked potentials of the median (sensory) and posterior tibial nerves were significantly prolonged when measured at the negative and positive deflections. The results suggest that, in addition to nerve conduction velocities, somatosensory evoked potential and distal latency are suitable measurements for detecting subclinical neurological damage among workers exposed to lead. As these changes were seen at blood lead concentrations of 2.35 μmol/l (48.7 μg/100 ml), there may be a need for more stringent monitoring of workers exposed to lead.

Lead Exposure and Nerve Conduction Velocity: The Differential Time Course of Sensory and Motor Nerve Effects

R. Singer, J.A. Valciukas, and R. Lilis. NEUROTOXICOLOGY (Park Forest, Il) 1983 Summer;4(2):193-202.

Authors' abstract: Nerve conduction velocities (NCV's) of the median motor, median sensory, peroneal motor, and sural nerves were measured on 40 lead-exposed automobile production workers as part of a comprehensive health survey. Blood lead (Pb-B) and blood zinc protoporphyrin (ZPP) were measured. The control group ($N = 31$) consisted of workers without lead exposure. All subjects were screened for the following conditions: Limb, neck, or back injury, diabetes, neurological disease, and alcohol consumption of more than 28 alcoholic beverages per week. Limb temperature was assessed at three sites for each NCV measurement. The lead-exposed workers had slower median sensory NCV (42.9 versus 46.8 m/sec, $p < 0.006$) and slower sural NCV (37.8 versus 42.8 m/sec, $p < 0.0004$). All NCV estimates were then statistically adjusted for age and temperature and transformed to Z values for further analyses. The mean standardized NCV's were slower in the lead-exposed group for the median sensory (-1.03 versus -0.04, $p < 0.0003$) and the sural nerves (-2.52

versus -0.52, $p < 0.001$). The study group was divided into two groups, with less than 10 years and more than 10 years of lead exposure. The subsample exposed less than 10 years showed slowing of the median sensory (-0.94 versus -0.04, $p < 0.005$) and the sural nerves (-2.42 versus -0.52, $p < 0.0001$). Pb-B and ZPP levels were correlated with sural velocity ($r = -0.54$, $p < 0.04$, and $r = -0.49$, $p < 0.06$, respectively). Mean Pb-B was 59.7 μg/dl and mean ZPP was 175.8 μg/dl. Workers exposed more than 10 years showed slowing of the median motor (-0.62 versus 0.91, $p < 0.02$), median sensory (-1.23 versus -0.04, $p < 0.0007$), and sural NCV (-2.70 versus -0.52, $p < 0.001$). ZPP levels were correlated with median and peroneal motor NCV ($r = -0.59$, $p < 0.03$, and $r = -0.75$, $p < 0.01$, respectively). Mean Pb-B = 60.6 μg/dl and mean ZPP = 160.1 μg/dl. A time course of effects is noted, whereby sensory NCV slowing seems to occur earlier than motor NCV slowing.

Electrophysiological Evaluation of Central and Peripheral Neural Effects of Lead Exposure

A.M. Seppalainen. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):43-52.

Author's abstract: Lead encephalopathy is more usual in children and has rarely been observed in adults. Peripheral neuropathy on the other hand is of more common occurrence among adults with occupational lead exposure and has been extensively studied with electrophysiological methods. Although encephalopathy often manifests itself with generalized seizures, usual electroencephalographic (EEG) findings have been diffuse slow wave abnormalities. Paroxysmal abnormalities, either focal or generalized spikes and/or sharp waves, have been detected in some patients. Evoked potential studies have lately been applied to children or adults with a relatively low level of lead exposure, and minor dose-dependent differences have appeared in comparison to control groups. Subclinical signs of peripheral neuropathy have been detected among human subjects with various levels of lead exposure. Nerve conduction velocities of lead workers have been generally lower, although the means have been within normal limits. Some authors have shown clear correlations between measures of lead exposure and nerve conduction velocities indicating an exposure-effect relationship.

Biochemical and Electrophysiological Study of Subjects with a History of Past Lead Exposure

G. Corsi, G.B. Bartolucci, P. Fardin, P. Negrin, and S. Manzoni. AM J IND MED 1984;6(4):281-90.

Authors' abstract: The effects of lead on porphyrin metabolism and peripheral nervous system were studied in a group of 38 subjects who had not been exposed for a period of time, ranging from 3 to 27 years. The mean values for blood lead (PbB), chelated lead (PbUEDTA), and free erythrocyte protoporphyrin (FEP) were found to be significantly higher in the subjects with past lead exposure than in controls. In all cases the neurological examination was negative. The mean values for maximum motor conduction velocity (MMCV) and conduction velocity of the slower fibers (CVSF) of the ulnar and peroneal nerves were found to be significantly lower in the subjects with past lead exposure than in the control group of 23 subjects standardized for age. Signs of partial denervation were present in four cases, with two presenting a decrease of the motor conduction velocity (MCV) as well. No correlation was found between electrophysiological findings and biochemical indicators of dose and effect. The length of exposure showed a significant negative correlation only with the MMCV of the ulnar nerve. A significant difference from controls standardized for age was observed only in subjects with exposure of more than 6 months for all the electromyographic (EMG) parameters. It does not appear that the EMG findings could depend upon modest lead deposits still present in the organism; they should rather give evidence to the permanent effect of alterations that occurred during the prolonged exposure to lead.

Neurophysiological Effects of Lead Exposure

I. Rosen, K. Wildt, B. Gullberg, and M. Berlin. SCAND J WORK ENVIRON HEALTH 1983 Oct;9(5):431-41.

Authors' abstract: A series of neurophysiological variables was measured for men occupationally exposed to lead. The results were related to the degree of lead exposure and to the concentrations of lead and zinc protoporphyrin in blood. A small but significant correlation was observed between lead exposure and motor and sensory conduction velocities in the lower limbs, the conduction velocities of slow motor fibers in the upper limbs, and also sensory nerve action potentials. It is suggested that a neurophysiological examination should be considered in the surveillance of the health of lead workers.

High Accuracy (Stable Isotope Dilution) Measurements of Lead in Serum and Cerebrospinal Fluid

W.I. Manton and J.D. Cook. BR J IND MED 1984 Aug;41(3):313-9.

Authors' abstract: The concentration of lead in blood, serum, cerebrospinal fluid, and urine was measured in patients with neurological disease and in control subjects, including cases of plumbism. A plot of blood lead

versus serum lead resembles the familiar curves of blood lead versus either free erythrocyte porphyrin or urinary δ-aminolevulinic acid, in that serum lead is constant up to a blood lead concentration of 40 μg/dl (2 μmol/l) and rises steeply thereafter. The serum lead concentrations yield renal clearances in the range 5-22 ml/min, in agreement with values obtained with radiolead on man and predicted from animal studies. The lead content of cerebrospinal fluid is consistently less than that of serum, averaging 50% of the serum concentration for blood leads of less than 20 μg/dl (1 μmol/l) but rising to 80%-90% in cases of plumbism. Patients with motor neuron disease could not be distinguished from those with other neurological diseases on the basis of the lead content of their serum or cerebrospinal fluid.

Lead in Cerebrospinal Fluid and Its Relationship to Plasma Lead in Humans

A. Cavalleri, C. Minoia, M. Ceroni, and M. Poloni. J APPL TOXICOL 1984 Apr;4(2):63-5.

Authors' abstract: Lead levels in whole blood, plasma, and cerebrospinal fluid (CSF) were determined in 18 patients suffering from amyotrophic lateral sclerosis (ALS) and in 21 subjects hospitalized for neurological investigations. No significant differences were found for blood, plasma, and CSF lead concentration between the ALS group and the other patient group. The plasma lead-CSF lead mean ratio was greater than 1 in both groups, whereas in subjects with a slight degree of blood-CSF barrier impairment a significant decrease of the ratio was demonstrated. A significant relationship between plasma lead and CSF lead levels ($r = 0.405$; $p < 0.01$), but not between whole blood lead and CSF lead levels, was established. Lead levels in CSF were also age-related ($r = 0.485$; $p < 0.05$) in the group of patients not suffering from ALS. In subjects with normal blood-brain barrier permeability, lead in plasma is a good indicator of CSF lead concentration.

Lead Concentrations in Blood, Plasma, Erythrocytes, and Cerebrospinal Fluid in Amyotrophic Lateral Sclerosis

T. Stober, W. Stelte, and K. Kunze. J NEUROL SCI 1983 Sep;61(1):21-6.

Authors' abstract: The purpose of the investigation was to elucidate the repeatedly discussed relationship between chronic lead intoxication and amyotrophic lateral sclerosis (ALS). The following mean lead concentrations were determined in 9 patients with ALS: 8.65 ± 3.91 μg/100 ml in the blood, 0.97 ± 0.78 μg/100 ml in the plasma, 19.15 ± 5.0 μg/100 ml in the erythrocytes, and 0.89 ± 0.44 μg/100 ml in the cerebrospinal fluid. These values did not differ appreciably from the controls with 7.91 ± 3.83 μg/100 ml ($n = 14$) in the blood, 1.13 ± 0.46 μg/100 ml ($n = 10$) in the plasma, 18.96 ± 12.63 μg/100 ml ($n = 10$) in the erythrocytes, and 0.85 ± 0.91 μg/100 ml ($n = 15$) in the cerebrospinal fluid. These findings do not support the assumption of lead poisoning as a pathogenetic factor in ALS.

Studies on Lead Pollution: Atomic Absorption Spectrophotometric Determination of Lead in Hair and Teeth Samples

A.K. Shrivastava and S.G. Tandon. INT J ENVIRON ANAL CHEM 1984;17(3-4):293-8.

Authors' abstract: A simple, rapid, and reliable method for the determination of lead in hair and teeth samples has been described. The method incorporates digestion of the samples by nitric acid, followed by atomic absorption spectrophotometric determination of lead using 283.3 nm wavelength.

Lead Levels Determined in Swedish Permanent Teeth by Particle-Induced X-Ray Emission

B. Moller, L.E. Carlsson, G.I. Johansson, K.G. Malmqvist, L. Hammarstrom, and M. Berlin. SCAND J WORK ENVIRON HEALTH 1982 Dec;8(4):267-72.

Authors' abstract: The determination of lead in permanent teeth is a useful measure of past exposure in early childhood since these teeth are mineralized in early childhood. Particle-induced X-ray emission (PIXE) analysis has been shown to be a method with good applicability for the contamination-free analysis of elements heavier than calcium in dental hard tissues. The method is rapid and nondestructive. The purpose of this study, which used the PIXE technique, was to survey the average level of lead in the coronal dentin of permanent bicuspid teeth collected in three places representing Swedish urban and rural areas. In addition, teeth from the New York City area were analyzed. The material comprised 165 teeth from Sweden and, for comparison, 14 teeth from New York City. The median value of lead in the Swedish teeth was 2.9 μg/g, a value indicating an insignificant influence from the environment in comparison with the New York teeth, for which the median value was 9.2 μg/g. There was, however, a statistically significant difference in the lead concentration of teeth from large and small Swedish cities; this finding may reflect different automobile traffic intensity.

Analysis of Lead in Circumpulpal Dentin of Deciduous Teeth

P. Grandjean, O.N Hansen, and K. Lyngbye. ANN CLIN LAB SCI 1984 Jul-Aug;14(4):270-5.

Authors' abstract: Absorbed lead continuously adds to the lead deposited in the vascularized circumpulpal den-

tin of the teeth. Thus, this dental tissue is expected to contain a lead concentration that reflects the integrated lead exposure during the time from completion of tooth formation to tooth extraction or shedding. A method has been developed to assess the lead level in the dentin surrounding the pulp chamber in deciduous teeth. Variation within the tooth is minimal, but upper medial incisors show a slightly lower lead level than do other incisors, as assessed in 714 teeth from first-grade Danish school children. This tendency was not confirmed, however, in a small number of paired teeth from the same children. The new method appears advantageous for epidemiological studies of lead neurotoxicity in children.

Reproducibility and Quality Control in the Analysis of Biological Samples for Lead and Mercury

B.E. Saltzman, D.W. Yeager, and B.G. Meiners. AM IND HYG ASSOC J 1983 Apr;44(4):263-7.

Authors' abstract: A simple statistical calculation was applied to 8 years of data on routine control sample and duplicate analyses from a laboratory quality control program. This provided standard deviations truly representative of this laboratory, at no additional analytical expense, and accurate information on how they varied with concentrations. From these, the detection limit of the method, upper warning limits, and upper control limits for differences between duplicate analyses were calculated. These values were conveniently used for quality control in determinations of lead in blood and of mercury in urine.

Innovative Modifications to the Delves Cup Blood-Lead Analysis Procedure

Y.P. Taylor. AM IND HYG ASSOC J 1984 Dec;45(12):B12, B14, B16.

Author's abstract: The Delves cup technique for blood-lead analysis involves the atomization of lead from a nickel cup into a ceramic tube and analysis by atomic absorption. The method is rapid and sensitive. The efficiency of the method is greatly affected by a few variables which, when controlled, have resulted in improved reproducibility and increased accuracy. The purpose of this paper is to address these variables.

Sampling and Analysis Techniques Used in a Blood Lead Survey of 1,241 Children in Port Pirie, South Australia

D.F. Sinclair and B.R. Dohnt. CLIN CHEM 1984 Oct;30(10):1616-9.

Authors' abstract: Methods are described for taking finger-prick blood samples and for analyzing these samples for lead. Quality-control techniques and procedures for the validation of all results are described. Results of a survey of 1,241 children are given and results for 149 venous samples are compared with results for the corresponding finger-prick samples. This finger-prick sampling method evidently is suitable for use in screening large numbers of children.

Effect of Bias in Hematofluorometer Measurements of Protoporphyrin in Screening Programs for Lead Poisoning

D.G. Mitchell and D. Doran. CLIN CHEM 1985 Mar;31(3):386-90.

Authors' abstract: Values for erythrocyte protoporphyrin (EP), measured in our laboratory after extraction with ethyl acetate-acetic acid, were compared with hematofluorometer measurements made in 21 other laboratories. We found that: (a) for samples of patients' blood, hematofluorometer results were 11% to 28% lower than the extraction-based values, depending on the concentration of EP and the mathematical model used; (b) hematofluorometers had mean errors of 0% to 3% for federal proficiency-testing samples; (c) there were no performance differences between fresh and shipped blood for the six laboratories that were analyzing both; (d) a hematofluorometer with a 20% low bias at an EP concentration of 500 μg per liter of whole blood (by the extraction method) will not detect about a third of the children whose EP concentration exceeds that cutoff value; and (e) at this same cutoff value for EP, the extraction test detects about 45% of children whose blood lead exceeds 300 μg/L, whereas a 20% low-bias hematofluorometer detects only about 37%.

Zinc Protoporphyrin as an Indicator for Occupational Lead Exposure

K. Kono, Y. Yoshida, A. Harada, Y. Takeda, M. Murao, and T. Hirota. BULL OSAKA MED SCH 1982 Jul;28(1):14-26.

Authors' summary: Concentrations of free erythrocyte protoporphyrin (FEP) and zinc protoporphyrin (ZnP) in the blood of lead-exposed workers were measured by the ethyl-acetate-acetic acid extraction method, ethanol extraction method, and hematofluorometric method. The validity of using ZnP was evaluated in a screening test for lead absorption among industrial workers. It was observed that workers chronically exposed to lead had both ZnP and protoporphyrin (PP) in different ratio in their blood. The ethanol extraction procedure by which ZnP and PP could be completely separated was used to evaluate the validity of using ZnP as a screening test for lead absorption. The results of the hematofluorometric determination were higher than the spectrofluorometric

values. In each method, a good relationship was obtained between ZnP value and blood lead concentration. A straight line relationship gave a ZnP value of 100 to 150 μg/100 ml for a corresponding blood lead concentration of 60 μg/100 ml in lead-exposed workers. The data indicated that the ZnP value obtained by hematofluorometer could be used as a screening test for chronic lead absorption, but further investigation is necessary to determine the biological threshold limit of ZnP in lead-exposed workers.

Free Erythrocyte Protoporphyrin and Zinc Protoporphyrin Measurements Compared as Primary Screening Methods for Detection of Lead Poisoning

B. Kaul, G. Slavin, and B. Davidow. CLIN CHEM 1983 Aug;29(8):1467-70.

Authors' abstract: We compared two commonly used primary screening methods (FEP and ZnP) for detecting Pb poisoning in children, used according to three major protocols. The results showed that FEP and ZnP values were comparable for only 36% of the children examined; 54% had FEP > ZnP and 10% had ZnP > FEP. One would identify approximately twice as many children with Pb > 300 μg/L by an FEP (500 μg/L cutoff) as with a ZnP (400 μg/L cutoff) screen. With a cutoff of 350, as compared with 500 μg/L for ZnP, one would perform 33% additional confirmatory blood Pb determinations with a 3% increased detection of Pb intoxication. If the number of false-negative Pb specimens is to be minimized, the cutoff "action level" for hematofluorometers should be lowered from the currently recommended 500 μg/L of whole blood to 350 μg/L. Our long experience and that of other laboratories leads us to recommend a revision of the Centers for Disease Control risk categories and cutoff values, depending on whether FEP or ZnP is measured in combination with a patient's blood Pb concentration. Our finding of above-normal values for ZnP and FEP with Pb concentrations < 300 μg/L indicates that iron deficiency constitutes an equally important public health problem for children in New York City.

Screening for Lead Toxicity Among Autobody Repair Workers

D.N. Rose, C.E. Cummings, J. Molinaro, and A. Fertig. AM J IND MED 1982;3(4):405-12.

Authors' abstract: Fifty-one workers in 10 small, neighborhood autobody repair shops were screened for lead toxicity by using blood zinc protoporphyrin (ZPP) levels and work history questionnaires. Those with high ZPP levels (> 50 μg/dl) had further studies, including blood lead determinations. The shops were dusty with ground putty dust (lead-free) and paint spray (lead content range, 0%-40%). Thirteen (26%) workers had mildly elevated ZPP levels (all were full-time sander/sprayers), though few had symptoms and none had elevated blood lead levels. Eighteen controls, workers in other occupations, had normal ZPP levels. Air monitoring during inactive periods failed to reveal high lead levels (range, 0-28 $\mu g/m^2$). These data suggest that workers in autobody repair shops are at risk of lead toxicity, but the exposure and biologic effects are less than in many other industries that utilize lead.

Temporal Stability of Blood Lead Concentrations in Adults Exposed Only to Environmental Lead

H.T. Delves, J.C. Sherlock, and M.J. Quinn. HUM TOXICOL 1984 Aug;3(4):279-88.

Authors' abstract: The temporal stability of blood lead concentrations of 21 healthy adults (14 men and 7 women) exposed only to environmental lead was assessed by analysis of 253 blood specimens collected serially over periods from 7 to 11 months. Improved analytical sensitivity allowed detection of small (< 1.0 μg/100 ml) changes in blood lead concentrations, and both within- and between-run analytical errors were minimized by a strict internal quality control protocol. The women had lower blood lead concentrations (mean 8.5, range 7.4-10.8 μg/100 ml) than did the men (mean 12.2, range 8.6-15.8 μg/100 ml). These are within the expected ranges for nonoccupationally exposed persons. Blood lead concentrations in the serial specimens from both men and women changed very little over the study period, with standard deviations of < 0.5 μg/100 ml for the majority of individual mean concentrations: for all except two subjects the standard deviations were < 0.8 μg/100 ml. Two subjects showed significant changes in blood lead concentrations during the study (standard deviations of mean > 1.0 μg/100 ml). A temporary increase in oral lead intake was identified for one of these subjects. In the absence of substantial changes in lead exposure blood lead levels in adults are remarkably stable, and for their environmental monitoring a single blood lead concentration is an excellent biological indicator.

Exposure to Lead and Cadmium of the General Population of Malta

P. Bruaux, F. Claeys-Thoreau, G. Ducoffre, A. Lafontaine, A. Grech, and A. Vassallo. INT ARCH OCCUP ENVIRON HEALTH 1983;53(2):119-25.

Authors' abstract: The blood levels of lead (PbB), cadmium (CdB), and zinc protoporphyrin (ZPP) were determined in 538 Maltese adult subjects. A relatively

high-level exposure to both metals was discovered. For lead, the median value is 274 μg/l with percentile 90 and 98, respectively, 564 and 863 μg/l. These values are to be compared with the reference values proposed by a directive of the European Community, respectively, 200, 300, and 350 μg/l. For cadmium, the median value is 2.2 μg/l with percentile 90 and 98, respectively, 3.8 and 5.7 μg/l. These values are compared with those of a Belgian population, which are, respectively, 1.7, 2.6, and 4.3 μg/l. The causes of this relatively high exposure are not known. A few tentative hypotheses, which are to be investigated, are made.

PbB and ALAD in Mentally Retarded and Normal Children

S. Telisman, D. Prpic-Majic, and T. Beritic. INT ARCH OCCUP ENVIRON HEALTH 1983;52(4):361-9.

From authors' abstract: Blood lead (PbB) and erythrocyte δ-aminolevulinic acid dehydratase (ALAD) were measured in a group (A) of 50 mentally retarded children whose illnesses were of unknown etiology (24 boys and 26 girls; average age 13.38 years, range 10-17 years) from an institution for handicapped children in Zagreb, and in a group (B) of 50 "normal" children (31 boys and 19 girls; average age 13.36 years, range 10-17 years) from a nearby orphanage in the same area (less polluted) of northern Zagreb. The children in group A had spent an average of 4.12 years (0.6-12 years) in the institution and came from both urban (n = 23) and rural (n = 27) areas. The children in group B had spent an average of 4.88 years (1-14 years) in the orphanage and also came from both urban (n = 38) and rural (n = 12) areas. The data obtained indicate a very close distribution of PbB levels in both groups, but a considerably different distribution of ALAD levels in favor of a lower activity in mentally retarded children. However, PbB and ALAD in both groups were within the range of currently acceptable "normal" values. The median and range values in groups A and B, respectively, were: 132 μg/l (85-256 μg/l) and 135 μg/l (78-215 μg/l) for PbB; 49.2 European units (27.0-65.0 European units) and 54.6 European units (27.0-69.9 European units) for ALAD.

Concentrations of Lead, Cadmium, and Zinc in Human Heart Muscle and Aorta After Acute Myocardial Infarction

M. Speich. J AM COLL NUTR 1982;1(3):255-62.

Author's abstract: Zinc, lead, and cadmium were measured in the myocardium (left and right ventricles) and aorta of 14 women and 12 men who had died from acute myocardial infarction (MI), and of 12 control women and 15 control men who had died of acute trauma. Mineral content of the necrotic areas of the MI patients was also determined. There was little significant correlation with age, and sex could not be shown to influence the cation concentrations. Significantly larger concentrations of lead and cadmium were observed in the right ventricle of women controls. In the four populations, significantly higher zinc concentrations were found in the left ventricle. Lead and cadmium levels in aortas were consistently higher than those in left ventricles, whereas zinc levels were always lower. The lead content in the ventricles and aorta of MI victims was consistently greater than for control subjects, though the difference was not significant. However, in the necrotic area, a significant decrease in zinc concentration was noted. These results are discussed and compared with other results published previously. It is concluded that studies in this area must be continued because there are still many uncertainties.

Blood Levels of Cadmium, Copper, Lead and Zinc in Children in a British Columbia Community

K.S. Subramanian and J.C. Meranger. SCI TOTAL ENVIRON 1983 Sep;30:231-44.

Authors' abstract: The levels of Cd, Cu, Pb, and Zn were measured in duplicate whole blood samples of 946 apparently normal children ranging in age from 2 years to 12 years and living in Kamloops, British Columbia, Canada. The metals were determined by using atomic absorption spectrometry (AAS): graphite furnace AAS for Cd and Pb, and flame AAS for Cu and Zn. The median and extreme values expressed as milligrams of metal per liter of whole blood for the total population were: Cd ≤ 0.0005; Cu, 1.11 (0.69-1.78); Pb, 0.112 (0.020-0.400); and Zn, 4.30 (2.10-6.53). No significant variations were noted in the median metal values either with age or with sex. The median Cu, Pb, and Zn values were within the normal range.

Lead and Cadmium Levels in Blood Samples from the General Population of Sweden

C.G. Elinder, L. Friberg, B. Lind, and M. Jawaid. ENVIRON RES 1983 Feb;30(1):233-53.

Authors' abstract: Lead and cadmium were determined in whole blood samples obtained from 473 nonoccupationally exposed adult persons in Sweden in 1980. Analyses were performed by using atomic absorption spectrophotometry equipped with an electrothermal atomization unit. Accuracy of the analysis was confirmed by the analysis of quality control samples. Blood lead concentrations were shown to be significantly influenced by sex, smoking habits, and alcohol consumption. Current male smokers had a median blood lead level of 92 μg Pb/liter, as compared with 77 μg Pb/liter for non-

smokers. For females the corresponding values were 69 μg Pb/liter and 57 μg Pb/liter for current smokers and nonsmokers, respectively. Highly significant correlations were found between stated alcohol consumption and blood lead in most of the different sex and smoking categories. People living in apartments close to streets with heavy traffic in Stockholm had slightly, but not significantly, higher blood lead levels when compared with people living in areas of this city with low traffic density. Blood cadmium levels were very strongly affected by smoking habits. A significant correlation existed between the number of cigarettes consumed daily and blood cadmium concentration. The median blood cadmium level for nonsmoking males was 0.2 μg Cd/liter (≤ 0.2, detection limit) and for females 0.3 μg Cd/liter. About 90% of all nonsmokers had cadmium concentrations in blood below 0.6 μg Cd/liter, whereas about 90% of the current male and female smokers had cadmium concentrations in blood of 0.6 μg Cd/liter or more.

Trace Analysis of Lead in Blood, Aluminium and Manganese in Serum and Chromium in Urine by Graphite Furnace Atomic Absorption Spectrometry

K.G. Brodie and M.W. Routh. CLIN BIOCHEM 1984 Feb;17(1):19-26.

Authors' abstract: A graphite furnace atomizer with automatic sampler is used to measure low levels of trace metals in biological samples by atomic absorption spectrometry. With blood and serum, the sample treatment consists of diluting (1:1) with aqueous Triton X-100 solution, centrifuging in the case of blood, and dispensing the liquid directly into a pyrolytic coated graphite tube. Sample volumes for blood and serum range from 5 to 10 μL. Stabilized urine (25 μL) is analyzed directly. The possibility of contamination is minimized by this simple procedure. The methods described minimize sample handling and involve reagents that are virtually free of contamination of the analytes. Background correction is necessary except for the determination of aluminium in serum, and precisions range from 0.7% to 4.3% RSD. The standard additions technique is used to establish the calibration, and the required volume of sample and aqueous addition is automatically dispensed directly into the graphite tube.

Effects of Blood and Urine on Lead Analyzed by Flameless Atomic Absorption

R.J. Shamberger. J CLIN CHEM CLIN BIOCHEM 1983 Feb;21(2):107-11.

Author's abstract: About a 10%-15% difference was observed by comparing (CDC) bovine blood to a lead standard addition curve with human blood. Results similar to the mean of the CDC survey were obtained by adding lead directly to the bovine blood by using standard addition techniques. These results indicate that standard additions of lead should be made to the same matrix and that matrix effects can occur when blood from different species is compared. Analyses of both CDC bovine blood and human blood with added Triton X-100 showed greater sensitivity and reproducibility than similar blood without added Triton X-100. $(NH_4)_2HPO_4$ greatly enhanced the signal height of lead in urine, whereas nitric acid had a much less effect. The enhancement by $(NH_4)_2HPO_4$ of the lead signal was at final concentrations $>$ 10 g/l. At $<$ 10 g/l enhancement rapidly decreased. Triton X-100 did not enhance the signal height of lead in urine. Calcium ion and chloride ion did not decrease the lead absorption peak in urine, but magnesium ion did decrease the height of the absorption peak in urine.

Determination of Diethyllead in the Urine by Flameless Atomic Absorption Spectrometry

Z. Turlakiewicz, M. Jakubowski, and J. Chmielnicka. BR J IND MED 1985 Jan;42(1):63-6.

Authors' abstract: A method for the determination of diethyllead in urine by flameless atomic absorption spectrometry after chelation with glyoxal-bis (2-hydroxyanil) and extraction of the formed complex with methyl isobutyl ketone is described. The method is specific in relation to both triethyllead and inorganic lead. The limit of detection was 3.2 μg Pb/l, and the relative standard deviation in the concentration range 20-100 μg Pb/l was 0.076.

Determination of Lead in Blood by Flame Atomic-Fluorescence Spectrometry

P.R. Sthapit, J.M. Ottaway, and G.S. Fell. ANALYST 1983 Feb;108(1283):235-43.

Authors' abstract: A simple, rapid method is described for the determination of lead in blood. Dilution 1 + 4 with Triton X is the only sample preparation required, and measurements are carried out by using a purpose-built atomic-fluorescence spectrometer with a nitrogen-separated air-acetylene flame. The preparation and operation of the lead electrodeless discharge lamps used as the excitation source have been optimized by a 10-factor Simplex procedure. A detection limit of 6 μg/l has been achieved for lead in aqueous solution. No significant chemical interferences were observed from the major constituents of the blood matrix, and a second continuum source is used to achieve automatic background correction for scattered radiation. Aqueous lead standards are used for calibration. Accuracy was established by satis-

factory comparison with values reported for quality control blood samples.

Hot Leaching of Ceramic and Enameled Cookware: Collaborative Study

J.H. Gould, S.W. Butler, K.W. Boyer, and E.A. Steele. J ASSOC OFF ANAL CHEM 1983 May;66(3):610-9.

Authors' abstract: A hot leach method published by the World Health Organization for determining lead (Pb) and cadmium (Cd) in ceramic and enameled ware was collaboratively studied in 14 laboratories. The method consisted of heating a solution of 4% acetic acid at the boil for 2 h in six samples of specially glazed ceramic ware and six samples of special enameled ware. The acid was allowed to cool and stand in contact with the ware for an additional 22 h. At the end of the 2-h heating period and again at the end of the 24-h period, the leach solution was assayed by atomic absorption spectrophotometry for Pb and Cd. Ruggedness testing before the collaborative study revealed that: (1) the quantity of metal released increased as the average leach temperature approached the boiling point, (2) the quantity of Pb and Cd released from enameled ware increased linearly with time during 7 h of boiling, (3) the concentration of acid could be varied from 2% to 6% with no apparent effect on the amount of metal released, and (4) the room temperature (RT) contact period lasting from 22 to 120 h (after the 2-h heating period) did not increase the amount of metal released. The quantities of Pb and Cd measured by the collaborators at the end of 2 h of heating and after 24 h of total contact were essentially identical. The amounts of Pb and Cd were not related to the quantity of acid solution required to restore the leach solution volume to its initial value after boiling. The collaborative results showed that the period of standing at RT is not necessary and probably can be eliminated from the method. The modified method, which requires analysis of the leach solution immediately after the 2-h heating period, has been adopted interim official first action by the Association of Official Analytical Chemists (AOAC).

The Effect of Container Material, Storage Time and Temperature on Cadmium and Lead Levels in Heparinized Human Whole Blood

K.S. Subramanian, J.C. Meranger, and J. Connor. J ANAL TOXICOL 1983 Jan-Feb;7(1):15-9.

Authors' abstract: The effect of container material (polycarbonate, polyethylene, polypropylene, polystyrene, borosilicate glass, and Pyrex glass), storage time (0, 1, 3, 6, 13, 20, 28, and 60 days), and temperature (22° C, 4° C, and −10° C) on cadmium and lead levels in heparinized human whole blood was studied by using graphite furnace atomic absorption spectrophotometry. Whole blood samples stored in polycarbonate containers at -10° C did not show significant change in the concentrations of cadmium and lead up to 60 days. Further, the cadmium and lead levels remained unchanged for 2 wk when the samples were stored in polyethylene and polypropylene vessels at 4° C.

Graphite Furnace Atomic Absorption Spectrometry with Matrix Modification for Determination of Cadmium and Lead in Human Urine

K.S. Subramanian, J.C. Meranger, and J.E. MacKeen. ANAL CHEM 1983 Jun;55(7):1064-7.

Authors' abstract: A diammonium hydrogen phosphate-nitric acid-graphite furnace atomic absorption spectrophotometric method and an ammonium nitrate-nitric acid-graphite furnace atomic absorption spectrophotometric procedure have been developed for determining nanogram per milliliter levels of cadmium (Cd) and lead (Pb), respectively, in human urine samples. Values for Cd in the sample are obtained by direct comparison with linear working curves prepared from aqueous standards in the diammonium hydrogen phosphate-nitric acid medium; there is no need to use the method of standard addition or matrix-matched calibration curves. In the case of Pb, matrix-matched calibration plots are essential. The detection limits (3 standard deviations of blank) for Cd and Pb are 0.9 and 4.1 ng/mL, respectively. Data are presented on the degree of accuracy and precision of the methods. At least 25 samples can be analyzed per hour. The sensitivity and simplicity of the procedures make them attractive for routine environmental surveillance involving large throughput of samples.

Oxygen Ashing and Matrix Modifiers in Graphite Furnace Atomic Absorption Spectrometric Determination of Lead in Whole Blood

D.K. Eaton and J.A. Holcombe. ANAL CHEM 1983 May;55(6):946-50.

Authors' abstract: An evaluation of the chemical and/or physical involvement of a number of matrix modifiers and procedures is presented for the determination of Pb in blood by graphite furnace atomic absorption. In particular, the roles of HNO_3, $NH_4H_2PO_4$, O_2 ashing, and surfactants (such as Triton-X 100) have been studied. Appearance time shifts and changes in peak shape are also presented. A rapid method for the determination of Pb in human whole blood by graphite furnace atomic absorption spectrometry is also described. Sample preparation involves dilution of whole red cells 1:4 with 1% Triton-X 100 solution, followed by an air ash. Oxygen ashing was used at 900 °C without any loss of Pb, no reduction in furnace lifetime, and negligible background scatter.

Determination of Lead in Whole Blood by Electrothermal Atomic-Absorption Spectrometry Using Graphite Probe Atomisation

S.K. Giri, C.K. Shields, D. Littlejohn, and J.M. Ottaway. ANALYST 1983 Feb;108(1283):244-53.

Authors' abstract: Atomisation from a pyrolytic graphite probe, placed in a hot and constant-temperature HGA 70 furnace, was used for the direct determination of lead in diluted whole blood. Substantial reductions in the classical vapor-phase interference effects by up to 2% m/V magnesium chloride and calcium chloride and 1.5% m/V sodium chloride allowed the use of aqueous standard solution for analytical calibration. Good agreement with national (UK) mean values was obtained for the analysis of quality control blood samples. The analytical precision is equivalent to that with conventional atomisation, but with improved sensitivity.

Determination of Lead in Bonemeal by Differential Pulse Anodic Stripping Voltammetry Using a Hydrochloric Acid Solubilization

R.D. Satzger, R.W. Kuennen, and F.L. Fricke. J ASSOC OFF ANAL CHEM 1983 Jul;66(4):985-8.

Authors' abstract: A safe, rapid method is described for the determination of lead in bonemeal. This method uses a hydrochloric acid solubilization performed under pressure, followed by determination by differential pulse anodic stripping voltammetry. This provides an alternative to a nitric-perchloric acid wet ash. Data obtained using both methods are compared. The mean recovery of a standard Pb spike was 99.2 ± 7%. The concentration of Pb in bonemeal ranged from 1.0 to 15.6 μg/g.

Development of a Quality Assurance Program for Determination of Ultratrace Background Levels of Lead and Cadmium in Raw Agricultural Crops by Differential Pulse Anodic Stripping Voltammetry

R.D. Satzger, E. Bonnin, and F.L. Fricke. J ASSOC OFF ANAL CHEM 1984 Nov-Dec;67(6):1138-40.

Authors' abstract: Data on the background levels of lead and cadmium in the food supply are essential in order to establish a baseline from which to evaluate the extent of contamination in transport, processing, industrial atmospheric particulate fallout, and soil treatment (e.g., fertilizers, sewage sludge, etc.). This requires the establishment of site selection and sampling criteria as well as the development of a rigorous analytical method capable of performing routine analyses of Pb and Cd at ultratrace levels. The method used in this study, which was published previously, was designed to provide high sample throughput with minimal contamination. This involved control and measurement of blank levels and the establishment of quality control procedures to maintain confidence in the accuracy and precision of the method.

Rapid Direct Determination of Lead in Evaporated Milk by Anodic Stripping Voltammetry Without Sample Pretreatment

E.W. Zink, R.A. Moffitt, and W.R. Matson. J ASSOC OFF ANAL CHEM 1983 Nov;66(6):1409-13.

Authors' abstract: The method presented describes the direct determination of lead (Pb) in evaporated milk in which the milk ashing step prior to analysis is eliminated. Digital instrument readout units are μg of Pb/milliliters of milk. Total analysis time after instrument calibration is < 3 min per sample. Range of the method is 0.05-1.0 ppm lead in milk, and precision of the method expressed by relative standard deviation of duplicate pairs ranged from 30% at 0.1 μg/mL to 3% at 1.0 μg/mL of lead in milk. The method compares favorably with the Association of Official Analytical Chemists' (AOAC) official first action anodic stripping voltammetric method (25.074). In addition, the method appears to work equally well for skim evaporated milk, sweetened condensed milk, and nonfat powdered dry milk when the latter two are reconstituted with water according to product label instructions. Recovery and interference studies are presented.

Direct Determination of Lead in Evaporated Milk and Apple Juice by Anodic Stripping Voltammetry: Collaborative Study

E.W. Zink, P.H. Davis, R.M. Griffin, W.R. Matson, R.A. Moffitt, and D.T. Sakai. J ASSOC OFF ANAL CHEM 1983 Nov;66(6):1414-20.

Authors' abstract: A method for the direct determination of lead in evaporated milk and in fruit juice with no prior sample digestion was successfully collaborated by 13 laboratories. The anodic stripping voltammetric (ASV) method studied consisted of adding 0.2-mL aliquots of evaporated milk or 0.3-mL aliquots of fruit juice to 2.9 mL of a dechelating reagent, Metexchange. The reagent-sample mixture is then analyzed for lead by ASV with no further sample preparation. Each collaborator received 24 samples, 2 each at 5 different levels (0.07-0.70 ppm for spiked evaporated milk and 0.09-0.87 ppm for spiked apple juice), along with duplicate practice samples of labeled lead content at each of 2 levels for each sample type. All unknowns were coded with random numbers. Approximately 69% of the reporting laboratories had never analyzed either evaporated milk or fruit juice for lead. Average time between receipt of samples and reporting of results was 1.6 days for all laboratories. The pooled variations between duplicate

determinations for apple juice and evaporated milk were 0.00059 and 0.00043, respectively. The method was adopted official first action for both fruit juice and evaporated milk.

Problems in the Determination of Erythrocyte Protoporphyrin by Ethyl Acetate-Acetic Acid Extraction

D. Doran and D.G. Mitchell. ANN CLIN BIOCHEM 1984 Mar;21(Pt 2):141-5.

Authors' abstract: Three problems with the ethyl acetate-acetic acid method of protoporphyrin analysis were identified: (1) protoporphyrin extraction from whole blood may yield low recoveries in comparison with extraction from prediluted blood; (2) recovery of protoporphyrin is low with some batches of ethyl acetate, but such unsatisfactory reagent can be identified by an iodide oxidation test; and (3) protoporphyrin standards prepared with deionized water may be unstable. However, glass-distilled water is satisfactory.

An Internal Standard for Porphyrin Analysis

R.E. Carlson, R. Sivasothy, D. Dolphin, M. Bernstein, and A. Shivji. ANAL BIOCHEM 1984 Aug 1;140(2):360-5.

Authors' abstract: The routine clinical analysis of the porphyrin precursors of heme requires an internal standard for determining the efficiency of the analytical procedure used. 2-Vinyl-4-hydroxymethyldeuteroporphyrin IX has been prepared as an internal standard. Its application to porphyrin analysis has been demonstrated by using high-performance liquid chromatographic resolution of the uroporphyrins to protoporphyrins in normal and porphyric urine.

Kinetics of Lead Following Intravenous Administration in Man

B.C. Campbell, P.A. Meredith, M.R. Moore, and W.S. Watson. TOXICOL LETT 1984 May;21(2):231-5.

Authors' abstract: Whole body retention of lead (Pb) and lead kinetics in blood, urine, and feces were determined over 2 weeks following intravenous administration of ^{203}Pb-labelled chloride to two subjects. Pb was retained with a biological half-life of 73 days (mean). After day 1, Pb excreted in urine and feces remained fairly constant at 1% and 0.3% of the administered dose, respectively. There was a daily loss of 0.5% by other routes. There was a rapid clearance of isotope from plasma with a half-life of 1 min (mean). At 60 min, 45% of the administered dose was in erythrocytes; this changed little over the 2 weeks.

The Effects of CaEDTA Injection on Lead, Zinc, Copper and ALAD in Erythrocyte, Plasma and Urine in Lead-Exposed Workers: A 24-H Observation

H. Aono and S. Araki. INT ARCH OCCUP ENVIRON HEALTH 1984;55(1):13-8.

Authors' abstract: To evaluate the effects of calcium disodium ethylenediamine tetraacetate (CaEDTA) on the concentrations of lead, zinc, and copper in plasma, erythrocyte, and urine, and the δ-aminolevulinic acid dehydratase (ALAD) activity in erythrocyte, we administered CaEDTA in 1-h intravenous infusion to 10 male gun metal founders with blood-lead concentration of 39 to 64 μg/dl (mean, 49 μg/dl). We found that the plasma concentration of lead, following a rapid rise within the first 3 h, fell temporarily to the level significantly lower than the initial level 19 h after start of the infusion. The plasma concentration of zinc fell to the minimal level 5 h after the infusion; and the erythrocyte concentration of zinc and the ALAD activity concurrently rose to the maximal level 5 h after the infusion. By contrast, no significant alteration was observed in the concentrations of copper in plasma and erythrocyte. The maximal level of urinary metal excretion was attained during the period between 1 and 2 h after start of CaEDTA infusion for lead; within 2 h for zinc; and between 2 and 4 h for copper. The urinary metal excretion returned to the initial level 14 to 24 h after infusion for zinc and copper; but lead excretion was still higher than the initial level during this period. The difference in the kinetics of the three metals following CaEDTA injection is discussed in the light of these findings.

Lead and Zinc Concentrations in Plasma, Erythrocytes, and Urine in Relation to ALA-D Activity After Intravenous Infusion of Ca-EDTA

N. Ishihara, S. Shiojima, and K. Hasegawa. BR J IND MED 1984 May;41(2):235-40.

Authors' abstract: Lead and zinc concentrations in plasma, erythrocytes, and urine, urinary aminolevulinic acid (ALA) concentration, and aminolevulinic acid dehydratase (ALA-D) activity in blood were studied for 4 hours in two male lead workers during and after a 1-hour infusion of Ca-EDTA 2Na. Urinary and plasma lead concentrations increased as a result of administering Ca-EDTA 2Na, and the ratios of lead concentrations in plasma to those in urine were greatly increased. The increase of plasma lead concentration was not due to the hemolytic effect of Ca-EDTA 2Na but was due to mobilized lead, rapidly excreted in the urine. ALA-D activity in blood increased at the end of the experiment with a transient decrease during the infusion of Ca-EDTA 2Na. As zinc concentrations in erythrocytes and plasma did not decrease during the infusion despite an increase in the

urinary excretion of zinc, the transient decrease of ALA-D activity was not due to a loss of zinc caused by Ca-EDTA 2Na. From the results of additional experiments in vitro, this transient decrease could be related neither to Ca-EDTA 2Na nor to lead in the blood.

Assessment of Lead Stores in Children: Validation of an 8-Hour $CaNa_2EDTA$ Provocative Test

M.E. Markowitz and J.F. Rosen. J PEDIATR 1984 Mar;104(3):337-41.

Authors' abstract: Twenty-four-hour $CaNa_2EDTA$ provocative tests for the assessment of lead stores were successfully performed in 36 asymptomatic children with mild to moderate undue lead absorption (blood lead concentration $\leq$ 69 μg/dl and erythrocyte protoporphyrin $\geq$ 50 μg/dl). By comparing lead excretion during the first 8 hours with that excreted during the entire 24-hour test, we have developed new criteria for defining positive outcomes. We suggest that the excretion of $\geq$ 200 μg lead per 8 hours or a ratio of urinary lead (μg)/$CaNa_2EDTA$ administered (mg) $\geq$ 0.70 after a single intramuscular injection of $CaNa_2EDTA$ (500 mg/m^2) can identify those children who will respond to chelation treatment with lead diuresis.

Depressed Excretion of 6 β-Hydroxycortisol in Lead-Toxic Children

P. Saenger, M.E. Markowitz, and J.F. Rosen. J CLIN ENDOCRINOL METAB 1984 Feb;58(2):363-7.

Authors' abstract: 6 β-Hydroxycortisol (6 β OHF) is a highly polar metabolite of cortisol, probably formed in the endoplasmic reticulum of hepatocytes by cytochrome P-450-dependent microsomal monoxygenases. Lead decreases the activity of cytochrome P-450-dependent microsomal hydroxylases in vivo and in vitro. To examine possible inhibitory effects of lead on 6 β OHF metabolism, we measured urinary 6 β OHF excretion in 26 children with mild to moderate increases in blood lead concentrations. Children were divided into two groups on the basis of their response to the EDTA provocative test. This test was used to assess the size of chelatable and potentially toxic lead stores in such children. Children with elevated urinary lead excretion after an EDTA provocative test, i.e. elevated tissue lead stores, had markedly decreased urinary excretion of 6 β OHF (178 $\pm$ 15 μg/m^2 X 24 h) compared with children who had negative tests (333 $\pm$ 40 μg/m^2 X 24 h; $P < 0.01$); their urinary cortisol excretion was not different from that of age-matched controls. These findings suggest that lead, at relatively low concentrations, may interfere with hepatic microsomal formation of a cortisol metabolite.

A Laboratory Evaluation of Wipe Testing Based on Lead Oxide Surface Contamination

C. Chavalitnitikul and L. Levin. AM IND HYG ASSOC J 1984 May;45(5):311-7.

Authors' abstract: Although wipe testing has been used extensively as a measure of surface contamination in industrial hygiene, few scientific studies have been reported to validate the procedure with respect to quantitative recovery, repeatability, or methodology. Consequently, a laboratory evaluation of wipe testing, with particular attention to the Occupational Safety and Health Administration (OSHA) procedure, was undertaken by using lead oxide dust as the test contaminant. A dust dispersion system was devised by using a Wright dust feeder to produce relatively uniform surface concentrations in an aerosol chamber. Wipe materials included moistened filter paper, commercial paper towels, adhesive paper labels, and adhesive tape. The quantitative recovery and repeatability of the wipe procedures were related to surface concentrations and the operational and material variables. Significant improvements in recoveries of up to 90% can be obtained with good repeatability for removable lead oxide dust on nonporous surfaces by using moist paper on a fixed test surface area. For porous surfaces, which show significantly lower recovery by all methods, adhesive sampling materials applied at maximum pressure provided an optimum recovery of 77%. The importance of reliable surface contamination measurements in assessing potential health hazards underscores the desirability of improving the demonstrated deficiencies of the OSHA and other wipe sampling procedures.

Total Contribution of Airborne Lead to Blood Lead

W.I. Manton. BR J IND MED 1985 Mar;42(3):168-72.

Author's abstract: A 9-year study of blood lead concentrations and isotope ratios carried out on a married couple shows that pulmonary deposition cannot account for all the airborne lead in blood; that lead from bone may comprise 70% of blood lead; and that during pregnancy blood lead may double because of mobilization of lead from bone.

The Determination of Lead in Environmental Air Using a Radioisotope X-Ray-Fluorescence Unit

H. Kostalas. INT J APPL RADIAT ISOT 1982 Dec;33(12):1475-6.

Author's abstract: The feasibility for the development of a portable radioisotope-excited X-ray fluorescence unit, able to detect lead (Pb) in air samples, was studied. The unit employs a 0.6-mCi ^{109}Cd source and an Xe-

filled proportional detector. The sensitivity of the method was found to be 15 μg of lead per cubic meter of air. Suggestions are also made for the improvement of the sensitivity.

Effect of Smoking on Cadmium and Lead Concentrations in Human Amniotic Fluid

C.P. Siegers, J.R. Jungblut, F. Klink, and F. Oberheuser. TOXICOL LETT 1983 Dec;19(3):327-31.

Authors' abstract: The amniotic fluids of 155 pregnant women, nonsmokers (n = 128) and smokers (n = 27), were investigated on their cadmium (Cd) and lead (Pb) concentrations. The mean ± s range of Cd in the amniotic fluid of nonsmokers amounted to 2.58 ± 1.36 ng/l, that of smokers to 7.29 ± 2.39 μg/l. Moreover, there was a correlation between the extent of daily cigarette consumption and Cd levels. With Pb, higher concentrations were found, ranging between 23.98 ± 9.41 ng/l for nonsmokers and 21.53 ± 7.16 μg/l for smokers. No correlations were seen between age, week of pregnancy, blood pressure, disorders of pregnancy, and the amniotic Cd or Pb concentrations. Thus, the maternal and fetal risks of the higher Cd levels in the amniotic fluid of smoking women remain unanswered.

Selenium and Other Elements in Human Maternal and Umbilical Serum, as Determined Simultaneously by Proton-Induced X-Ray Emission

M. Hyvonen-Dabek, P. Nikkinen-Vilkki, and J.T. Dabek. CLIN CHEM 1984 Apr;30(4):529-33.

Authors' abstract: Using PIXE (proton-induced X-ray emission), we simultaneously determined the concentrations of Se, Ca, Fe, Cu, Zn, Br, and Pb in blood serum from 56 pregnant women, 25 healthy controls, and 31 others with twin pregnancy or some complicating condition (diabetes, hypertension, epilepsy, hepatosis gravidarum, pre-eclampsia, small baby), and in cord-blood serum from 21 newborns. Pellets, pressed from the serum samples after yttrium had been added as an internal standard, and after mixing, and then evaporation at 30° C with or without reduced pressure (< 1 kPa), were bombarded by 2.2 MeV protons from a Van de Graaff accelerator in the air and the induced X-rays collected by a Ge(Li) detector. Relative to mean Se values for early 6- to 12-week pregnancy (0.045 ppm), those for 35- to 42-week pregnancy (0.028 ppm) were low ($p < 0.001$). Umbilical cord blood serum showed even lower values (0.016 ppm, $p < 0.001$) — findings in harmony with the incidence pattern of Keshan cardiomyopathy. Pb crossed the placenta; values for cord serum were not significantly different from those in pregnancy serum. Cu, Zn, Fe, and Ca showed the significant expected patterns in the different groups. Compared with the late-pregnancy controls, Fe was high in mothers of small-birth-weight babies (1.70 ppm, $p < 0.02$). Br was high in pre-eclampsia (3.59 ppm, $p < 0.05$) and mothers with twins (3.61 ppm, $p < 0.05$).

Lead, Erythrocyte Protoporphyrin, and Ferritin Levels in Cord Blood

B. Kaul, B. Davidow, Y.M. Eng, and M.H. Gewirtz. ARCH ENVIRON HEALTH 1983 Sep-Oct;38(5):296-300.

Authors' abstract: A pilot study was initiated to examine cord blood from approximately 300 newborns of various ethnic groups from two New York City hospitals for lead (Pb), erythrocyte protoporphyrin (EP), ferritin (FRT), and hemoglobin (Hb) levels during 1979 and 1980. Results showed an overall mean Pb level of 8 ± 4 μg/dl, EP level of 61 ± 26 μg/dl [geometric mean (GM) = 66.36], FRT level of 165 ± 107 ng/ml (GM = 135.99), and a distribution frequency of Hb with nearly 69% between 13.5 and 16.9 g % (mean ± standard deviation = 15 ± 1), 20% below 13.4 g % (12 ± 2 g %), and 11% at or above 17.0 g % (18 ± 1 g %). Both EP and FRT showed a bimodal distribution. There was a negative correlation between blood EP and plasma FRT levels that was significant at the .03% level. The study also showed that a significant drop in mean cord blood Pb levels occurred compared with earlier studies. Followup of newborns with mildly elevated Pb and EP levels should be made, and screening of mothers for Pb levels during early pregnancy should constitute a part of prenatal care, particularly for those from urban areas with previously demonstrated environmental Pb hazard.

Iron Depletion and Blood Lead Levels in a Population with Endemic Lead Poisoning

C. Hershko, A.M. Konijn, J. Moreb, G. Link, F. Grauer, and E. Weissenberg. ISR J MED SCI 1984 Nov;20(11):1039-43.

Authors' abstract: The effect of iron depletion on blood lead levels was studied in a group of 558 schoolchildren aged 10 to 18 residing in two West Bank Arab villages with a high prevalence of excessive lead exposure and clinical lead poisoning. Thirty percent of the subjects studied had whole-blood lead levels > 30 μg/dl, and 45% had whole-blood zinc erythrocyte protoporphyrin > 50 μg/dl. The percentage of abnormal blood lead values in subjects with normal serum ferritin and transferrin saturation (31%) was similar to that in subjects with one (28%) or two (25%) abnormal iron parameters. Likewise, there was no correlation between serum ferritin and blood lead levels in individual patients ($r = 0.059$). Normal distribution plots and mean levels of blood lead (27.3 μg/dl) were identical in the iron-

deficient and iron-replete groups. These findings indicate that iron depletion does not affect blood lead levels and suggest that in man, unlike in experimental animals, iron depletion may not have a significant effect on lead absorption.

Developmental Changes in Erythrocyte Protoporphyrin: Roles of Iron Deficiency and Lead Toxicity

R. Yip and P.R. Dallman. J PEDIATR 1984 May;104(5):710-3.

Authors' abstract: Iron deficiency and lead toxicity both result in increased erythrocyte protoporphyrin (EP). The purpose of this study was to determine the differences in EP concentration, according to age and sex, obtained in the Second National Health and Nutrition Examination Survey of the United States and to determine the extent to which EP differences might be related to iron deficiency or lead toxicity. The highest EP concentrations were found in infants and children. Among adults, women had higher EP values than men. Lead toxicity (blood lead $>$ 30 μg/dl) and low serum iron concentration/total iron binding capacity (Fe/TIBC $<$ 16%), often in combination, were associated with elevated EP values in infants and children. In women, elevated EP concentrations were related primarily to low Fe/TIBC values, whereas in men there was only a weak association with elevated blood lead concentration. Age/sex differences in EP values diminished markedly when the influences of lead toxicity and iron deficiency were excluded by the above criteria.

Prevalence and Causes of Anemia in the United States, 1976 to 1980

P.R. Dallman, R. Yip, and C. Johnson. AM J CLIN NUTR 1984 Mar;39(3):437-45.

Authors' abstract: We estimated the prevalence of anemia in the United States from the results of the Second National Health and Nutrition Examination Survey (NHANES II, 1976 to 1980). Reference ranges for hemoglobin (Hb) were first derived from 11,547 subjects in whom laboratory values for serum iron/iron-binding capacity, mean corpuscular volume, and erythrocyte protoporphyrin were all normal ($\geq$ 16%, $\geq$ 80 fl, and $\leq$ 75 μg/dl red blood cells, respectively). With these reference standards, the prevalence of anemia (Hb values below the 95% reference range for age and sex) among the 15,093 subjects with complete laboratory results was highest in infants (5.7%), teenage girls (5.9%), young women (5.8%), and elderly men (4.4%). The pattern of laboratory abnormalities in anemic subjects indicated that iron deficiency predominated as a cause in infants and young women in contrast to inflammatory disease in the elderly.

Iron Deficiency in Health and Disease

J.D. Reeves, E. Vichinsky, J. Addiego, Jr., and B.H. Lubin. ADV PEDIATR 1983;30:281-320.

Authors' abstract: Iron deficiency is a common problem in otherwise healthy children and in children with systemic disease. We have reviewed the pathophysiology, laboratory diagnosis, and systemic effects of iron deficiency. We have emphasized that routine screening procedures do not efficiently predict those otherwise healthy children who will demonstrate a therapeutic response to iron. Furthermore, in patients with certain systemic diseases the diagnosis of iron deficiency is complicated by the inflammatory process, and the response to a therapeutic trial of oral iron is often blunted. Since the potential adverse effects of iron deficiency may be extensive, a therapeutic trial of iron is indicated to establish the diagnosis of iron deficiency if the index of suspicion is high and laboratory results are equivocal.

Diagnosis of Anemia and Iron Deficiency: Analytic and Biological Variations of Laboratory Tests

P.R. Dallman. AM J CLIN NUTR 1984 Jun;39(6):937-41.

Author's abstract: We describe the magnitude of analytic errors and the within-subject biological variations for laboratory tests that are used in the diagnosis of anemia and iron deficiency. For hemoglobin (Hb), hematocrit, and red cell indices, coefficients of variation for analytic and biological variations are $<$ 4%. In general, higher coefficients of variation are characteristic of serum iron, iron-binding capacity, serum ferritin, and erythrocyte protoporphyrin. Particularly high analytic variations between different laboratories have been described for iron-binding capacity, and the greatest biological variations have been noted for serum iron. An awareness of these sources of error is helpful in designing studies and in interpreting laboratory results.

Free Erythrocyte Protoporphyrin (FEP) I. Normal Values for Adults and Evaluation of the Hematofluorometer

W.L. Marsh, Jr., D.P. Nelson, and H.M. Koenig. AM J CLIN PATHOL 1983 Jun;79(6):655-60.

Authors' abstract: Since the early 1970's, measurement of free erythrocyte protoporphyrin (FEP) (by microextraction or by hematofluorometer) has been widely used to screen for lead poisoning and to evaluate microcytic red blood cell (RBC) disorders in children. However, published information on normal values for FEP, performance of the hematofluorometer, and usefulness of FEP in classifying microcytic RBC disorders in

adults is scant. In an adult population with normal hematocrit and mean corpuscular volume (MCV) and normal values for serum ferritin, blood lead level, and serum bilirubin, we obtained normal hematofluorometer FEP levels of < 30 μg/dL for men, and < 40 μg/dL levels for women. We have evaluated a hematofluorometer against a standard microextraction procedure and feel that the hematofluorometer is superior for clinical laboratories if elevated FEP's are confirmed by retesting with washed RBC. In the second part of this paper, we demonstrate the usefulness of the FEP in classifying microcytic RBC disorders in adults.

Free Erythrocyte Protoporphyrin (FEP) II. The FEP Test Is Clinically Useful in Classifying Microcytic RBC Disorders in Adults

W.L. Marsh, Jr., D.P. Nelson, and H.M. Koenig. AM J CLIN PATHOL 1983 Jun;79(6):661-6.

Authors' abstract: Microcytic red blood cells (RBC) are commonly encountered in clinical medicine and are caused by disorders of heme synthesis [usually iron deficiency anemia (IDA) or anemia of chronic disease (ACD)] or disorders of globin synthesis (usually thalassemia syndromes or HbE). Using the clinical history and standard laboratory tests (hematocrit, per cent saturation of transferrin (% sat), serum ferritin, Hb electrophoresis, HBA_2, and HbF), we classified 198 adults with microcytic RBC as follows: 48 IDA, 11 probable IDA, 11 iron-deficient erythropoiesis without anemia, 13 ACD, 42 α-thalassemia trait, 35 probable α-thalassemia trait, 20 β-thalassemia trait, and 15 unclassified. In addition, we demonstrated that the FEP test reliably (83%-90% of the time, depending on FEP methodology) classifies microcytic RBC states into disorders of heme synthesis versus disorders of globin synthesis. Because of reliability and ease of measurement, we recommend the hematofluorometer FEP as the first step in the clinical laboratory evaluation of microcytic RBC disorders in both adults and children.

Screening for Iron Deficiency with the Erythrocyte Protoporphyrin Test

R. Yip, S. Schwartz, and A.S. Deinard. PEDIATRICS 1983 Aug;72(2):214-9.

Authors' abstract: Elevation of erythrocyte protoporphyrin (EP) level is one of the consequences of iron deficiency. Since the EP test has been established as a screening test for lead poisoning, the screening capability of the EP test for iron deficiency was investigated. A total of 4,160 children between ages 6 months to 12 years had EP determined together with serum ferritin and hematocrit. When we compared the relationship of EP to serum ferritin and used a serum ferritin value ≤ 15 μg/L as the criterion of iron deficiency, the optimal cutoff limit for the EP test appears to be 35 μg/dL of whole blood. At this level, 88% of the subjects with low levels of serum ferritin can be detected (sensitivity), in contrast to the 53% detected at a higher cutoff value (≥ 50 μg/dL) used to screen for lead toxicity, or to the 59% detected by age-related hematocrit value. At an EP screening level of 35 μg/dL of whole blood, 90% of the subjects with normal serum ferritin level are correctly determined to be screen negative (specificity). The predictive value of low levels of serum ferritin for all subjects above screening level is 38%. In general, an elevated EP level, by itself, represents inadequate iron supply for hematopoiesis and signals iron deficiency regardless of whether the serum ferritin value is below the diagnostic level or not. A trial course of orally administered iron is suggested for children who are found to have an elevated EP value, with an increase in hemoglobin or hematocrit value serving, retrospectively, as confirmation of prior iron deficiency.

Free Erythrocyte Protoporphyrin as an Index of Perinatal Iron Status

S.K. Chong, M.J. Thompson, J.E. Shaw, and D. Barltrop. J PEDIATR GASTROENTEROL NUTR 1984 Mar;3(2):224-9.

Authors' abstract: The relationship between free erythrocyte protoporphyrin and conventional indices of iron status was studied in 49 mothers and their infants. Maternal venous blood samples were collected at 34 weeks' gestation and at delivery. The corresponding infant blood samples were collected from the umbilical cord and at age 6 weeks. In each case free erythrocyte protoporphyrin, serum iron, total iron binding capacity, and serum ferritin were determined. Cord free erythrocyte protoporphyrin was negatively correlated with maternal ferritin at 34 weeks' gestation ($p = 0.016$) and at delivery ($p = 0.014$), and with transferrin saturation at delivery ($p = 0.026$). The infants' hemoglobin concentrations at 6 weeks were significantly negatively related to maternal free erythrocyte protoporphyrin at 34 weeks ($p = 0.026$) and at delivery ($p = 0.026$). Cord free erythrocyte protoporphyrin is an index of maternal iron status in the last trimester. Maternal free erythrocyte protoporphyrin in the last trimester predicts the magnitude of physiological anemia of the infant at age 6 weeks.

Iron Status of the Preterm Infant During the First Year of Life

H.L. Halliday, T.R. Lappin, and G. McClure. BIOL NEONATE 1984;45(5):228-35.

Authors' abstract: The iron status of 49 preterm infants (mean gestational age, 33.1 weeks) was assessed serially

during the 1st year of life. Hemoglobin concentration, serum ferritin, serum transferrin, serum iron, and transferrin saturation were measured on nine occasions in each infant. In 16 infants of gestational age 28-32 weeks, the hemoglobin concentration was significantly lower at 3, 6, and 9 weeks when compared with 33 infants of gestational age 33-36 weeks. For all other measures of iron status, there were no significant differences between these gestational age groups. For the entire group of 49 infants, the mean hemoglobin concentration reached a nadir of 11.2 g/dl at 9 weeks. Mean serum iron and transferrin saturation reached peaks of 24 μmol/l and 65%, respectively, at 3 weeks. The mean serum ferritin remained over 100 μg/l until after 18 weeks. Thirteen infants (26%) had iron deficiency defined as either serum ferritin < 10 μg/l ($n = 10$) or transferrin saturation $<$ 10% ($n = 5$) or both ($n = 3$).

Free Erythrocyte Protoporphyrin Levels in the First Year of Life

H.D. Heese, W.S. Dempster, and F. Pocock. S AFR MED J 1983 Aug 13;64(7):237-9.

Authors' abstract: Free erythrocyte protoporphyrin (FEP) levels were measured in 161 infants judged not to be iron-deficient. In addition to high mean FEP levels in cord blood, a significant number of infants had FEP levels in excess of 120 μg/dl red blood cells during the first 6 months of life. These levels are comparable to those found in iron-deficient adults. It is concluded that the clinical significance of an FEP level in excess of 120 μg/dl and its value as a marker of early iron deficiency during the first 6 months of life require further study. FEP values in excess of 120 μg/dl were not observed in infants aged 7-12 months.

Iron Deficiency in Infants: The Influence of Mild Antecedent Infection

J.D. Reeves, R. Yip, V.A. Kiley, and P.R. Dallman. J PEDIATR 1984 Dec;105(6):874-9.

Authors' abstract: In this study of 467 healthy term infants seen for routine 1-year health maintenance examination, we determined the influence of mild prior infection on the concentration of hemoglobin (Hgb) and other laboratory evidence of iron deficiency. In addition we studied the Hgb response in 261 infants randomized to receive a 3-month course of treatment with either iron or placebo. Infants who had had one or more clinic visits because of infection during the previous 3 months or who were reported as not being entirely well during the past month or who had an elevated sedimentation rate were more likely to have anemia or "low normal" Hgb, higher erythrocyte protoporphyrin and serum ferritin values, and lower serum iron concentration than infants who had been well. Hgb response ≥ 1 g/dl after iron treatment occurred more commonly in infants who had prior visits because of infection. The results indicated that upper respiratory and other mild antecedent infections commonly predispose to iron deficiency (probably because of a decrease in iron absorption).

The Prevalence of Iron Deficiency in Apparently Healthy Cape Coloured Infants

G.F. Kirsten, H.D. Heese, S. de Villiers, W.S. Dempster, H.E. Varkevisser, and M. Hoffman. S AFR MED J 1984 Mar 10;65(10):378-80.

Authors' abstract: To obtain a more accurate picture of the prevalences of anemia, iron deficiency anemia, hematological iron deficiency, and diminished iron stores, we studied 240 Cape colored infants from the lower socioeconomic groups. Anemia was diagnosed in 42 infants (17.5%), iron deficiency anemia in 81 (34%), and hematological iron deficiency in 28%; 64 (27%) showed evidence of diminished iron stores. The findings indicate that iron deficiency was a common problem in the infants studied, and the same probably also applies to the community at large.

Developmental Changes in Serum Ferritin and Erythrocyte Protoporphyrin in Normal (Nonanemic) Children

A.S. Deinard, S. Schwartz, and R. Yip. AM J CLIN NUTR 1983 Jul;38(1):71-6.

Authors' abstract: We studied 4,039 children who were 6 mo to 12 yr of age to characterize developmental variations of serum ferritin and erythrocyte protoporphyrin. Age-related descriptive statistics were derived. The -2 SD value for serum ferritin was found to increase progressively from 12 to 21 μg/l with increasing age, and the +2 SD value for erythrocyte protoporphyrin was found to decrease progressively from 65 to 42 μg/dl whole blood with increasing age. Although the mean serum ferritin value was found to continue to rise throughout the first 12 yr of life, erythrocyte protoporphyrin values were highest at 1 to 2 yr of age, then fell to essentially constant levels after 4 to 6 yr of age. These relationships, as well as the linear relationship of increasing hematocrit and serum ferritin with increasing age, suggest that the rise of hematocrit with age, as previously observed, is associated with improving storage and availability of iron for heme synthesis.

Serum Ferritin in Evaluation of Iron Status in Children

F. Madanat, M. El-Khateeb, M. Tarawaneh, and S. Hijazi. ACTA HAEMATOL (Basel) 1984;71(2):111-5.

Authors' abstract: The value of serum ferritin in assessing iron status was studied in 192 preschool age

children between the ages of 3 and 60 months. Children were considered to have iron deficiency if the transferrin saturation was less than 16% and the peripheral smear revealed microcytosis and hypochromia. Anemia was present when the hemoglobin level was 10.5 g/dl. According to this criteria, 46% of children screened had either iron deficiency (11.5%) or iron deficiency anemia (34.4%). Mean serum ferritin for the iron deficiency anemia group was 39.1 ng/mg as compared with 41.7 ng/ml for the iron deficiency group and 84.7 ng/ml for the normal group. Even though the serum ferritin level was lower in the iron deficiency group, the difference in the means did not reach statistical significance. Furthermore, only 30% of children who had either iron deficiency or iron deficiency anemia had a serum ferritin level of less than 12 ng/ml, the level considered diagnostic for iron deficiency. It can be concluded that serum ferritin cannot be used alone for iron status determination. Multiple parameters will make the assessment more reliable.

Application of Receiver-Operator Analysis to Diagnostic Tests of Iron Deficiency in Man

I. Kim, E. Pollitt, R.L. Leibel, F.E. Viteri, and E. Alvarez. PEDIATR RES 1984 Sep;18(9):916-20.

Authors' abstract: The objective of the present report is to demonstrate the use of receiver-operator characteristics (ROC) analysis in the selection of diagnostic tests for iron deficiency in a specific population. Conventional ROC curves were prepared with true positive fraction (TPF) and false positive fraction (FPF) determined by the application of different cut-off points for four indicators of iron status. ROC plots were then transformed into normal deviate scales. The advantages of Gaussian transformation of TPF and FPF when underlying decision functions are normally distributed are: the ROC curve is a straight line; and the separation between the two distributions and shape of these distributions can be simply quantitated as intercepts and slopes. In the present study, pretreatment hemoglobin concentration was the most robust diagnostic indicator of iron deficiency, as operationally defined by a response of hemoglobin to iron treatment. Free erythrocyte protoporphyrin was a more sensitive and specific predictor than either serum ferritin or transferrin saturation when a stringent operational definition of iron deficiency was used. These findings illustrate the utility of ROC analysis in discriminating between diagnostic indicators having different degrees of accuracy.

Clinical Evaluation of Iron Deficiency

J.D. Cook. SEMIN HEMATOL 1982 Jan;19(1):6-18.

Author's abstract: Although the prevalence of iron deficiency has remained relatively constant, there has been continuing refinement in its laboratory recognition, especially with the recent introduction of serum ferritin and FEP [free erythrocyte protoporphyrin] measurements. It is helpful to classify iron deficiency into three stages. Storage iron depletion is identified by marrow examination or serum ferritin, iron deficient erythropoiesis by TS [transferrin saturation], FEP, or MCV [mean corpuscular volume], and iron deficiency anemia by hemoglobin concentration or therapeutic iron trial. Combinations of these measurements have been used in prevalence studies to obtain a quantitative measure of body iron stores. The optimal laboratory approach to diagnosing iron deficiency depends on the clinical setting. In the office or outpatient clinic, iron depletion is best recognized by the serum ferritin, although the TS, FEP, and MCV are helpful in gauging its severity. In hospitalized patients with overt anemia, the TS, FEP, and MCV are much less helpful because similar changes are seen in the anemia of chronic disease. Examination of marrow iron remains the method of choice, especially in patients with infection, chronic disease, malignancy, or liver disease, although in many clinical situations the same information can be obtained from a serum ferritin. Serial measurements of serum ferritin have been particularly useful in monitoring patients at high risk of iron deficiency such as those with rheumatoid arthritis, chronic inflammatory bowel disease, or chronic renal failure.

Erythrocyte and Plasma Ferritin in Normal Subjects, Blood Donors and Iron Deficiency Anemia Patients

H.H. Bodemann, A. Rieger, K.J. Bross, H. Schroter-Urban, and G.W. Lohr. BLUT 1984 Mar;48(3):131-7.

Authors' abstract: Ferritin concentration has been determined with an immunoradiometric assay in plasma and washed sedimented erythrocytes after hypotonic lysis. There was a gradual decrease of plasma ferritin in the sequence normal males, normal females, blood donors, and patients with iron deficiency anemia. Erythrocyte ferritin remained unchanged in normal males and females and in blood donors, but dropped significantly in the anemic patients. Correspondingly, the ratio of erythrocyte to plasma ferritin rose from less than 2 in healthy males up to 8 in persons with iron deficiency. Little, if any, effect on plasma and erythrocyte ferritin was observed in 12 male and female volunteers when taking iron for 4 weeks. In two patients with iron deficiency anemia the blood counts were normalized within 2-3 months during oral iron substitution, accompanied by a drastic increase of the erythrocyte ferritin concentration to values far above normal. In contrast, the plasma ferritin concentration remained below normal. Thus, in iron deficiency, erythrocyte ferritin is synthesized with priority in the presence of iron and, in addition

to plasma ferritin, appears to be a useful parameter of the iron status.

Basic Ferritin Content of Red Cells of Patients with Anemia and Polycythemia Vera

M.B. Van der Weyden, H. Fong, L.J. Hallam, and M.J. Breidahl. PATHOLOGY 1984 Oct;16(4):419-23.

Authors' abstract: Basic ferritin content of red cells has been evaluated with a simplified assay in subjects with various erythroid disorders. In 39 patients with iron deficiency anemia, red cell ferritin was significantly reduced compared with that of normal individuals. Thirty percent of these patients had low normal red cell ferritin content, and the mean corpuscular volume (MCV) for this group was significantly higher than that of patients with reduced red cell ferritin. The mean red cell ferritin of 30 subjects with the anemia of chronic disease was significantly reduced, and patients in this group with normal red cell ferritin had higher plasma ferritin levels. In 14 patients with polycythemia vera, the mean red cell ferritin was significantly reduced and showed a positive correlation with the hemoglobin level and percent transferrin saturation. The red cell ferritin content of 9 individuals with acquired immune hemolytic anemia and 10 with acquired sideroblastic anemia was significantly elevated and, in subjects with immune hemolysis, showed a positive correlation with the reticulocyte count. These findings suggest a lack of discriminatory function for red cell ferritin in iron deficiency anemia and anemia of chronic disease. Evaluation of this parameter in the individual patient should take into account the presence of reticulocytosis.

The Value of the Peripheral Blood Smear in Anemic Inpatients. The Laboratory's Reading v a Physician's Reading

P. Jen, B. Woo, P.E. Rosenthal, H.F. Bunn, A. Loscalzo, and L. Goldman. ARCH INTERN MED 1983 Jun;143(6):1120-5.

Authors' abstract: Since physicians are routinely taught to review the peripheral blood smear results of all anemic patients, we analyzed the diagnostic value of the laboratory's blood smear reading and the incremental value of a physician's personal reading in anemic inpatients. Blood smear abnormalities, as reported by the laboratory and two hematologists, were poorly reproducible, with only 5 of the 11 types of abnormalities being more reproducible than could be expected by chance. The blood smear performed no better than red blood cell (RBC) indices in detecting probable iron deficiency or low serum levels of folate or vitamin B_{12}. In anemias not caused by deficiency states, the blood smear reading performed by the hospital laboratory provided unique information in 6% of the cases and helpful information in another 25%, but the additional reading performed by a hematologist never provided unique information and provided incremental helpful information in only 4% of the cases. The peripheral blood smears of all anemic inpatients should be read by the hospital laboratory, but in our hospital a routine additional personal reading by a physician had limited incremental value and could be reserved for selected cases.

Evaluation of Iron Status in Patients on Chronic Hemodialysis: Relative Usefulness of Bone Marrow Hemosiderin, Serum Ferritin, Transferrin Saturation, Mean Corpuscular Volume and Red Cell Protoporphyrin

J. Moreb, M.M. Popovtzer, M.M. Friedlaender, A.M. Konijn, and C. Hershko. NEPHRON 1983; 35(3): 196-200.

Authors' abstract: The diagnostic usefulness of bone marrow hemosiderin, serum ferritin, transferrin saturation, mean corpuscular volume (MCV), and red cell protoporphyrin (EPP) in the evaluation of iron status in patients on chronic hemodialysis was studied in 39 subjects. The correlation between serum ferritin and the number of transfusions received per month was slightly higher ($r = 0.717$; $p < 0.001$) than the correlation between bone marrow hemosiderin and transfusions ($r = 0.685$; $p < 0.01$). Serum ferritin was useful in identifying subjects with both increased or reduced iron stores. In contrast, transferrin saturation could only be used for indicating iron overload. MCV for indicating iron deficiency and EPP was not useful in either case. The abnormal increase of EPP in chronic uremia has not been previously described. It is unrelated to iron deficiency and is most probably explained by the known reduction in red cell ferrochelatase activity associated with chronic uremia. Serum ferritin is clearly the most useful diagnostic aid for assessing iron stores in patients on chronic hemodialysis. Whether ferritin is also the best predictor of response to iron therapy cannot be determined on the basis of the present data.

Iron Status and Anemia in the Elderly: New Findings and a Review of Previous Studies

P.J. Garry, J.S. Goodwin, and W.C. Hunt. J AM GERIATR SOC 1983 Jul;31(7):389-99.

Authors' abstract: Iron status was determined in 280 free-living and healthy elderly men ($n = 131$) and women ($n = 149$) by assessing dietary and supplemental iron intake as well as 10 biochemical measures of iron nutriture (erythrocyte count, hemoglobin level, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration,

plasma iron level, total iron-binding capacity, per cent transferrin saturation, and ferritin level). Subject ages ranged from 60 to 93 years with a median age of 72 years for both women and men. For comparison purposes, iron status measures in an unselected group of younger men (n = 107) and women (n = 164) between the ages of 20 and 39 years were also obtained. None of the elderly women and only two (1.2%) of the younger women had low hemoglobin levels (< 12.0 g/dl). Three (2.3%) of the elderly men and none of the younger men had low hemoglobin levels (< 14 g/dl). Other iron status measures revealed that anemia or iron deficiency was no more prevalent in the healthy elderly population than in the younger adult population when identical criteria were used to assess iron nutriture. The genesis of anemia often seen in the elderly is not completely understood. Reported evidence suggests the presence of anemia in the elderly is a result of overall reduction of hematopoietic reserves. Because of the potentially serious consequences of this assumption about anemia to the treatment of the elderly, the authors critically review some of the studies that have been designed in the past to determine the prevalence and etiology of anemia in the aged. They suggest that health status, race, socioeconomic status, diet, and region are more important than age as explanations for the high prevalence of anemia seen in many previous studies.

Iron Status of Elderly Americans

S.R. Lynch, C.A. Finch, E.R. Monsen, and J.D. Cook. AM J CLIN NUTR 1982 Nov;36(5 Suppl):1032-45.

Authors' abstract: Studies of iron nutriture in the elderly are limited, and very few include observations on individuals over the age of 75. The two Health and Nutrition Examination Surveys carried out by the U.S. Department of Health, Education and Welfare demonstrate that the mean iron intake of Americans is adequate until the age of 75. However, with changes in the major food sources there is a decrease in iron derived from meat and a concomitant rise in the proportion supplied by breakfast cereals. Alterations in dietary iron bioavailability that may result from this have not been studied. Physiological data suggest that the elderly do not represent a target population for iron deficiency, since iron requirements are no greater than those of adult men and lower than those of children and menstruating women. Furthermore, there is little direct evidence of a high prevalence of iron deficiency in the elderly, but the laboratory measurements that have proved useful in defining iron status in younger people have not been standardized for or extensively used in older people. Anemia is still the most important known consequence of significant iron deficiency. However, the application of hemoglobin (Hb) or hematocrit standards used in younger people to the elderly as well as the assumption that anemia can be equated with iron deficiency invalidates the conclusions of many surveys. Hb and hematocrit measurements are not suitable screening tests for iron deficiency in the elderly, and there is an urgent need for a clearer understanding of the physiological and nutritional factors responsible for lower Hb values in older people, particularly older blacks.

Sodium Chloride Pica Secondary to Iron-Deficiency Anemia

M.D. Shapiro and S.L. Linas. AM J KIDNEY DIS 1985 Jan;5(1):67-8.

Authors' abstract: A young woman was referred for nephrologic evaluation of hypertension and a curious desire for table salt. Suspicion of iron-deficiency anemia arose only after it was determined that sodium balance was achievable during supervised sodium restriction. This salt craving abated within 2 weeks of initiation of iron replacement therapy. Although pica is a common manifestation of iron deficiency, this appears to be the first reported case of salt pica secondary to iron deficiency.

A Small-Dose Iron Tolerance Test as an Indicator of Mild Iron Deficiency

W.H. Crosby and M.A. O'Neil-Cutting. JAMA 1984 Apr 20;251(15):1986-7.

Authors' abstract: Small doses of iron (5 to 20 mg) were used to study absorption in normal and mildly iron-deficient men. Plasma iron concentration was measured before and at frequent intervals after ingestion of iron. Men with normal iron stores showed little change in plasma iron levels, whereas mildly iron-deficient men showed large increases. This consistent observation of increases in plasma iron levels indicates that the iron tolerance test using small doses of iron is a sensitive indicator of iron deficiency. It provides a means of studying iron absorption without the use of radioactive tracers.

Erythrocyte Zinc Protoporphyrin (ZPP) in Subjects with Heterozygote β-Thalassemia, Acquired Non-Microcytic Anemias and Iron Deficiency

S. Cocuzza and G. Avola. BOLL SOC ITAL BIOL SPER 1984 Nov 30;60(11):2171-8.

Authors' abstract: The authors examine the utility of the zinc protoporphyrin level in blood (ZPP) as a diagnostic test for some anemias with different etiology. Our results show that the observed ZPP rise, both in sideropenic anemia and lead poisoning, is related to an

increase in total iron-binding capacity. This relation demonstrates that in both these anemias a close correlation exists with disorders of iron metabolism. Furthermore, such a correlation is not seen in thalassemic trait and in acquired nonmicrocytic anemias.

Thalassemia Among Chinese-Bostonians. Usefulness of the Hemoglobin H Preparation

E.S. Choi and T.F. Necheles. ARCH INTERN MED 1983 Sep;143(9):1713-5.

Authors' abstract: Microcytosis was noted in 14.7% of the complete blood cell count reports of Chinese subjects in a Boston Chinatown health center. One hundred forty-nine of these subjects' conditions were further evaluated by hemoglobin (Hb) electrophoresis, Hb H inclusion bodies preparation, Hb A_2 quantitation, and ferritin assay. Ninety-one cases of α-thalassemia-1 trait and 49 cases of β-thalassemia trait were diagnosed. In this study population, the prevalence of thalassemia trait and of iron deficiency resulting in microcytosis was 13.8% and 3.4%, respectively. The Hb H preparation was found to be clinically useful and reliable for detecting α-thalassemia-1 trait in Chinese carriers, after the exclusion of iron deficiency and β-thalassemia by routine studies.

SELECTED BIBLIOGRAPHY

Aguilar EM, Sanchez-Anzaldo FJ, Zuniga-Charles MA, Martinez Morales M, Arrieta ND, Molina-Regio NY, Molina Ballesteros G. Statistical correlation between δ-aminolevulinic acid dehydratase activity and blood lead in exposed and non-exposed human populations. A tentative model. ARCH INVEST MED (Mex) 1984 Apr-Jun;15(2):93-107.

Ahmad SH, Amir M, Ansari Z, Ahmed KN. Influence of maternal iron deficiency anemia on the fetal total body iron. INDIAN PEDIATR 1983 Sep;20(9):643-6.

Ahmad SH, Ansari Z, Matto GM, Amir M, Mallick A, Sharma SK, Ahmad KN, Husain I. Serum iron in babies of anemic mothers — II. INDIAN PEDIATR 1984 Oct;21(10):759-63.

Ahmad SH, Matto GM, Amir M, Ansari Z, Mallick MA, Sharma SK, Husain I, Ahmad KN. Hematological profile of babies of anemic mothers — I. INDIAN PEDIATR 1984 Oct;21(10):753-8.

Angle CR, Swanson MS, Stohs SJ, Markin RS. Abnormal erythrocyte pyrimidine nucleotides in uremic subjects. NEPHRON 1985;39(3):169-74.

*Aono H, Araki S. The effects of CaEDTA injection on lead, zinc, copper and ALAD in erythrocyte, plasma and urine in lead-exposed workers: a 24-h observation. INT ARCH OCCUP ENVIRON HEALTH 1984;55(1):13-8.

Araki S, Murata K, Yokoyama K, Yanagihara S, Niinuma Y, Yamamoto R, Ishihara N. Circadian rhythms in the urinary excretion of metals and organic substances in "healthy" men. ARCH ENVIRON HEALTH 1983 Nov-Dec;38(6):360-6.

Bachman K, Olkis A, Klenk H. A new method for the determination of 210Pb in natural samples. HEALTH PHYS 1984 May;46(5):1131-4.

*Batuman V, Landy E, Maesaka JK, Wedeen RP. Contribution of lead to hypertension with renal impairment. N ENGL J MED 1983 Jul 7;309(1):17-21.

Bellotti V, Bergamaschi G, Caldera D, Cazzola M, Ciriello MM, Colotti MT, Dezza L, Melzi D'Eril G, Quaglini S. Clinical evaluation of erythrocyte zinc-protoporphyrin as a parameter of iron status in man. HAEMATOLOGICA (Pavia) 1984 May-Jun;69(3):272-84.

Biosca M, Garcia-Bragado F, de la Figuera M, Madrenas J, Salas A. Carcinoid tumor, atrophic gastritis, and iron deficiency anemia [letter]. ANN INTERN MED 1985 Mar;102(3):416-7.

*Bodemann HH, Rieger A, Bross KJ, Schroter-Urban H, Lohr GW. Erythrocyte and plasma ferritin in normal subjects, blood donors and iron deficiency anemia patients. BLUT 1984 Mar;48(3):131-7.

*Boudene C, Despaux-Pages N, Comoy E, Bohuon C. Immunological and enzymatic studies of erythrocytic δ-aminolevulinate dehydratase. Comparison of results obtained in normal and lead-exposed subjects. INT ARCH OCCUP ENVIRON HEALTH 1984;55(1):87-96.

Bratton GR, Zmudzki J. Laboratory diagnosis of Pb poisoning in cattle: a reassessment and review. VET HUM TOXICOL 1984 Oct;26(5):387-92.

*Brodie KG, Routh MW. Trace analysis of lead in blood, aluminium and manganese in serum and chromium in urine by graphite furnace atomic absorption spectrometry. CLIN BIOCHEM 1984 Feb;17(1):19-26.

*Bruaux P, Claeys-Thoreau F, Ducoffre G, Lafontaine A, Grech A, Vassallo A. Exposure to lead and cadmium of the general population of Malta. INT ARCH OCCUP ENVIRON HEALTH 1983;53(2):119-25.

*Campbell BC, Meredith PA, Moore MR, Watson WS. Kinetics of lead following intravenous administration in man. TOXICOL LETT 1984 May;21(2):231-5.

Canfield PJ, Fairburn AJ, Watson AD. Blood lead, urinary δ-aminolevulinic acid and the diagnosis of lead poisoning in dogs. AUST VET J 1984 Oct;61(10):323-4.

*Carlson RE, Sivasothy R, Dolphin D, Bernstein M, Shivji A. An internal standard for porphyrin analysis. ANAL BIOCHEM 1984 Aug 1;140(2):360-5.

*Cavalleri A, Minoia C, Ceroni M, Poloni M. Lead in cerebrospinal fluid and its relationship to plasma lead in humans. J APPL TOXICOL 1984 Apr;4(2):63-5.

Centers for Disease Control. Preventing lead poisoning in young children — United States. MMWR 1985 Feb 8;34(5):66-8, 73.

Chakraborti D, De Jonghe WR, Van Mol WE, Van Cleuvenbergen RJ, Adams FC. Determination of ionic alkyllead compounds in water by gas chromatography/atomic absorption spectrometry. ANAL CHEM 1984 Dec;56(14):2692-7.

Chalevelakis G, Tsiroyannis K, Hatziioannou J, Arapakis G. Screening for thalassaemia and/or iron deficiency: evaluation of some discrimination functions. SCAND J CLIN LAB INVEST 1984 Feb;44(1):1-6.

*Abstracted

*Chavalitnitikul C, Levin L. A laboratory evaluation of wipe testing based on lead oxide surface contamination. AM IND HYG ASSOC J 1984 May;45(5):311-7.

*Cheson BD, Rom WN, Webber RC. Basophilic stippling of red blood cells: a nonspecific finding of multiple etiology. AM J IND MED 1984;5(4):327-34.

*Choi ES, Necheles TF. Thalassemia among Chinese-Bostonians. Usefulness of the hemoglobin H preparation. ARCH INTERN MED 1983 Sep;143(9):1713-5.

*Chong SK, Thompson MJ, Shaw JE, Barltrop D. Free erythrocyte protoporphyrin as an index of perinatal iron status. J PEDIATR GASTROENTEROL NUTR 1984 Mar;3(2):224-9.

Christensen DJ. Differentiation of iron deficiency and the anemia of chronic disease. J FAM PRACT 1985 Jan;20(1):35-9.

*Christoffersson JO, Schutz A, Ahlgren L, Haeger-Aronsen B, Mattsson S, Skerfving S. Lead in finger-bone analysed in vivo in active and retired lead workers. AM J IND MED 1984;6(6):447-57.

*Cocuzza S, Avola G. Erythrocyte zinc protoporphyrin (ZPP) in subjects with heterozygote β-thalassemia, acquired non-microcytic anemias and iron deficiency. BOLL SOC ITAL BIOL SPER 1984 Nov 30;60(11):2171-8.

Conley CL. Anemia: accurate diagnosis and appropriate therapy. HOSP PRACT [Off] 1984 Sep;19(9):57-66.

*Cook JD. Clinical evaluation of iron deficiency. SEMIN HEMATOL 1982 Jan;19(1):6-18.

Corsi G, Bartolucci GB. Biological monitoring of workers with past lead exposure. Biochemical findings. SCAND J WORK ENVIRON HEALTH 1982 Dec;8(4):260-6.

*Corsi G, Bartolucci GB, Fardin P, Negrin P, Manzoni S. Biochemical and electrophysiological study of subjects with a history of past lead exposure. AM J IND MED 1984;6(4):281-90.

*Craswell PW, Price J, Boyle PD, Heazlewood VJ, Baddeley H, Lloyd HM, Thomas BJ, Thomas BW. Chronic renal failure with gout: a marker of chronic lead poisoning. KIDNEY INT 1984 Sep;26(3):319-23.

*Crosby WH, O'Neil-Cutting MA. A small-dose iron tolerance test as an indicator of mild iron deficiency. JAMA 1984 Apr 20;251(15):1986-7.

Cullen MR, Robins JM, Eskenazi B. Adult inorganic lead intoxication: presentation of 31 new cases and a review of recent advances in the literature. MEDICINE (Baltimore) 1983 Jul;62(4):221-47.

Dabeka RW. Collaborative study of a graphite-furnace atomic-absorption screening method for the determination of lead in infant formulas. ANALYST 1984 Oct;109(10):1259-63.

*Dallman PR. Diagnosis of anemia and iron deficiency: analytic and biological variations of laboratory tests. AM J CLIN NUTR 1984 Jun;39(6):937-41.

Dallman PR. Manifestations of iron deficiency. SEMIN HEMATOL 1982 Jan;19(1):19-30.

*Dallman PR, Yip R, Johnson C. Prevalence and causes of anemia in the United States, 1976 to 1980. AM J CLIN NUTR 1984 Mar;39(3):437-45.

Daniel WW, Wees SJ. Intra-articular milk of calcium in saturnine gout. RADIOLOGY 1983 May;147(2):389-92.

*Deinard AS, Schwartz S, Yip R. Developmental changes in serum ferritin and erythrocyte protoporphyrin in normal (nonanemic) children. AM J CLIN NUTR 1983 Jul;38(1):71-6.

DeLuca SA. Lead poisoning. AM FAM PHYSICIAN 1984 Jul;30(1):179-80.

*Delves HT, Sherlock JC, Quinn MJ. Temporal stability of blood lead concentrations in adults exposed only to environmental lead. HUM TOXICOL 1984 Aug;3(4):279-88.

deSilva PE. Blood lead levels and the haematocrit correction. ANN OCCUP HYG 1984;28(4):417-28.

*DiMaio VJ, DiMaio SM, Garriott JC, Simpson P. A fatal case of lead poisoning due to a retained bullet. AM J FORENSIC MED PATHOL 1983 Jun;4(2):165-9.

Dine MS. What is the best test for iron deficiency? [letter]. PEDIATRICS 1983 Dec;72(6):909-10.

*Doran D, Mitchell DG. Problems in the determination of erythrocyte protoporphyrin by ethyl acetate-acetic acid extraction. ANN CLIN BIOCHEM 1984 Mar;21(Pt 2):141-5.

*Doss M, Baumann H, Lorrek M, Laubenthal F, Schneider J. Lead poisoning as a toxogenetic disease. KLIN WOCHENSCHR 1984 May 2;62(9):430-1.

*Doss M, Laubenthal F, Stoeppler M. Lead poisoning in inherited δ-aminolevulinic acid dehydratase deficiency. INT ARCH OCCUP ENVIRON HEALTH 1984;54(1):55-63.

Dreiling BJ, Steinberg MH. Neglected iron deficiency. J MISS STATE MED ASSOC 1984 Sep;25(9):231-3.

Drueke T, Touam M, Lacour B. Possible relation between RBC protoporphyrin and aluminum intoxication? [letter]. NEPHRON 1984;38(4):280.

Duggan MJ. The uptake and excretion of lead by young children. ARCH ENVIRON HEALTH 1983 Jul-Aug;38(4):246-7.

*Eaton DK, Holcombe JA. Oxygen ashing and matrix modifiers in graphite furnace atomic absorption spectrometric determination of lead in whole blood. ANAL CHEM 1983 May;55(6):946-50.

*Abstracted

*Elinder CG, Friberg L, Lind B, Jawaid M. Lead and cadmium levels in blood samples from the general population of Sweden. ENVIRON RES 1983 Feb;30(1):233-53.

Eschbach JW. Iron kinetics in healthy individuals and in chronic renal insufficiency. CONTRIB NEPHROL 1984;38:129-34.

Fell GS. Lead toxicity: problems of definition and laboratory evaluation. ANN CLIN BIOCHEM 1984 Nov;21(Pt 6):453-60.

Finch CA, Cook JD. Iron deficiency. AM J CLIN NUTR 1984 Mar;39(3):471-7.

*Fischbein A, Thornton JC, Sarkozi L, Kon S, Levin S. Subjective symptoms in workers with low-level exposure to lead. J APPL TOXICOL 1982 Dec;2(6):289-93.

Forsyth DS, Marshall WD. Determination of alkyllead salts in water and whole eggs by capillary column gas chromatography with electron capture detection. ANAL CHEM 1983 Nov;55(13):2132-7.

*Garry PJ, Goodwin JS, Hunt WC. Iron status and anemia in the elderly: new findings and a review of previous studies. J AM GERIATR SOC 1983 Jul;31(7):389-99.

Gillooly M, Torrance JD, Bothwell TH, MacPhail AP, Derman D, Mills W, Mayet F. The relative effect of ascorbic acid on iron absorption from soy-based and milk-based infant formulas. AM J CLIN NUTR 1984 Sep;40(3):522-7.

*Giri SK, Shields CK, Littlejohn D, Ottaway JM. Determination of lead in whole blood by electrothermal atomic-absorption spectrometry using graphite probe atomisation. ANALYST 1983 Feb;108(1283):244-53.

Gonzalez-Fernandez E, Gonzalez Moreno P. Screening analysis for lead in whole blood and urine by Delves cup method using quality control samples. Comparison with the dithizone method. IND HEALTH 1983;21(2):91-105.

*Gould JH, Butler SW, Boyer KW, Steele EA. Hot leaching of ceramic and enameled cookware: collaborative study. J ASSOC OFF ANAL CHEM 1983 May;66(3):610-9.

*Grandjean P. Lead poisoning: hair analysis shows the calendar of events. HUM TOXICOL 1984 Jun;3(3):223-8.

*Grandjean P, Hansen ON, Lyngbye K. Analysis of lead in circumpulpal dentin of deciduous teeth. ANN CLIN LAB SCI 1984 Jul-Aug;14(4):270-5.

Grandjean P, Holst E. Occupational health screening for lead exposure by the ZPP method. UGESKR LAEGER 1983 Sep 19;145(38):2960-3.

Grobler SR, Maresky LS, Rossouw RJ. Blood lead levels in marathon runners [letter]. S AFR MED J 1984 Jun 2;65(22):872-3.

Gurney JM. Anaemia and the Caribbean. J TROP PEDIATR 1983 Apr;29(2):76-80.

Hallberg L. Iron balance and iron deficiency in the elderly. BIBL NUTR DIETA 1983;(33):107-12.

Halliday HL, Lappin TR, McClure G. Cow's milk and anemia in preterm infants. ARCH DIS CHILD 1985 Jan;60(1):69-70.

*Halliday HL, Lappin TR, McClure G. Iron status of the preterm infant during the first year of life. BIOL NEONATE 1984;45(5):228-35.

Hansen TM, Hansen NE, Birgens HS, Hlund B, Lorenzen I. Serum ferritin and the assessment of iron deficiency in rheumatoid arthritis. SCAND J RHEUMATOL 1983;12(4):353-9.

*Healy MA, Aslam M, Harrison PG, Fernando MP. Lead-induced convulsions in young infants — A case history and the role of GABA and sodium valproate in the pathogenesis and treatment. J CLIN HOSP PHARM 1984 Sep;9(3):199-207.

*Heese HD, Dempster WS, Pocock F. Free erythrocyte protoporphyrin levels in the first year of life. S AFR MED J 1983 Aug 13;64(7):237-9.

*Hershko C, Konijn AM, Moreb J, Link G, Grauer F, Weissenberg E. Iron depletion and blood lead levels in a population with endemic lead poisoning. ISR J MED SCI 1984 Nov;20(11):1039-43.

Hodges DJ, Skelding D. Determination of lead in blood by atomic-absorption spectroscopy with electrothermal atomisation. ANALYST 1983 Jul;108(1288):813-20.

Horiguchi S, Kiyota I, Teramoto K, Kageyama M, Tojo F, Nakaseko H. Health examination with liver function tests of lead workers. OSAKA CITY MED J 1983;29(1):93-7.

Huat LH, Zakariya D, Eng KH. Lead concentrations in breast milk of Malaysian urban and rural mothers. ARCH ENVIRON HEALTH 1983 Jul-Aug;38(4):205-9.

Huebers H, Finch CA. Clinical aspects of iron deficiency. SEMIN HEMATOL 1982 Jan;19(1):3-5.

*Hyvonen-Dabek M, Nikkinen-Vilkki P, Dabek JT. Selenium and other elements in human maternal and umbilical serum, as determined simultaneously by proton-induced X-ray emission. CLIN CHEM 1984 Apr;30(4):529-33.

*Ishihara N, Shiojima S, Hasegawa K. Lead and zinc concentrations in plasma, erythrocytes, and urine in relation to ALA-D activity after intravenous infusion of Ca-EDTA. BR J IND MED 1984 May;41(2):235-40.

Ishikawa K, Narita O, Saito H. Gestational anemia and serum ferritin. KAKU IGAKU 1984 Apr;21(4):305-10.

*Abstracted

*Janin Y, Couinaud C, Stone A, Wise L. The "lead-induced colic" syndrome in lead intoxication. SURG ANNU 1985;17:287-307.

Janus ED, Hinton D, Colls BM. Red cell versus whole blood lead [letter]. NZ MED J 1983 Aug 10;96(737):633-4.

*Jen P, Woo B, Rosenthal PE, Bunn HF, Loscalzo A, Goldman L. The value of the peripheral blood smear in anemic inpatients. The laboratory's reading v a physician's reading. ARCH INTERN MED 1983 Jun;143(6):1120-5.

*Jeyaratnam J, Devathasan G, Ong CN, Phoon WO, Wong PK. Neurophysiological studies on workers exposed to lead. BR J IND MED 1985 Mar;42(3):173-7.

Johnson CS, Tegos C, Beutler E. Thalassemia minor: routine erythrocyte measurements and differentiation from iron deficiency. AM J CLIN PATHOL 1983 Jul;80(1):31-6.

*Kaul B, Davidow B, Eng YM, Gewirtz MH. Lead, erythrocyte protoporphyrin, and ferritin levels in cord blood. ARCH ENVIRON HEALTH 1983 Sep-Oct;38(5):296-300.

*Kaul B, Slavin G, Davidow B. Free erythrocyte protoporphyrin and zinc protoporphyrin measurements compared as primary screening methods for detection of lead poisoning. CLIN CHEM 1983 Aug;29(8):1467-70.

Keate RF, DiPietrantonio PJ, Randleman ME. Occupational lead exposure. ANN EMERG MED 1983 Dec;12(12):786-8.

Keogh JP. Recognizing lead poisoning in adults. ARCH INTERN MED 1984 Oct;144(10):1944-5.

*Kim I, Pollitt E, Leibel RL, Viteri FE, Alvarez E. Application of receiver- operator analysis to diagnostic tests of iron deficiency in man. PEDIATR RES 1984 Sep;18(9):916-20.

King E. Changes in blood lead concentrations in women in Wales 1972-82 [letter]. BR MED J [Clin Res] 1983 Jun 25;286(6383):2059-60.

*Kirkby H, Nielsen CJ, Nielsen VK, Gyntelberg F. Subjective symptoms after long term lead exposure in secondary lead smelting workers. BR J IND MED 1983 Aug;40(3):314-7.

*Kirsten GF, Heese HD, de Villiers S, Dempster WS, Varkevisser HE, Hoffman M. The prevalence of iron deficiency in apparently healthy Cape coloured infants. S AFR MED J 1984 Mar 10;65(10):378-80.

*Kono K, Yoshida Y, Harada A, Takeda Y, Murao M, Hirota T. Zinc protoporphyrin as an indicator for occupational lead exposure. BULL OSAKA MED SCH 1982 Jul;28(1):14-26.

*Kostalas H. The determination of lead in environmental air using a radioisotope X-ray-fluorescence unit. INT J APPL RADIAT ISOT 1982 Dec;33(12):1475-6.

Lackey CJ. Pica during pregnancy. BOL ASOC MED PR 1984 Sep;76(9):405-7.

Lim HW, Poh-Fitzpatrick MB. Hepatoerythropoietic porphyria: a variant of childhood-onset porphyria cutanea tarda. Porphyrin profiles and enzymatic studies of two cases in a family. J AM ACAD DERMATOL 1984 Dec;11(6):1103-11.

*Lynch SR, Finch CA, Monsen ER, Cook JD. Iron status of elderly Americans. AM J CLIN NUTR 1982 Nov;36(5 Suppl):1032-45.

*Madanat F, El-Khateeb M, Tarawaneh M, Hijazi S. Serum ferritin in evaluation of iron status in children. ACTA HAEMATOL (Basel) 1984;71(2):111-5.

Mannino S. Potentiometric stripping analysis of lead and tin with a continuous flow system. ANALYST 1984 Jul;109(7):905-7.

Mannino S. Simultaneous determination of lead and tin in fruit juices and soft drinks by potentiometric stripping analysis. ANALYST 1983 Oct;108(1291):1257-60.

*Manton WI. Total contribution of airborne lead to blood lead. BR J IND MED 1985 Mar;42(3):168-72.

*Manton WI, Cook JD. High accuracy (stable isotope dilution) measurements of lead in serum and cerebrospinal fluid. BR J IND MED 1984 Aug;41(3):313-9.

Manton WI, Kirkpatrick JB, Cook JD. Does the choroid plexus really protect the brain from lead? [letter]. LANCET 1984 Aug 11;2(8398):351.

*Markowitz ME, Rosen JF. Assessment of lead stores in children: validation of an 8-hour $CaNa_2EDTA$ provocative test. J PEDIATR 1984 Mar;104(3):337-41.

*Marsh WL Jr, Nelson DP, Koenig HM. Free erythrocyte protoporphyrin (FEP): I. Normal values for adults and evaluation of the hematofluorometer. AM J CLIN PATHOL 1983 Jun;79(6):655-60.

*Marsh WL Jr, Nelson DP, Koenig HM. Free erythrocyte protoporphyrin (FEP): II. The FEP test is clinically useful in classifying microcytic RBC disorders in adults. AM J CLIN PATHOL 1983 Jun;79(6):661-6.

Medeiros DM, Pellum LK. Elevation of cadmium, lead, and zinc in the hair of adult black female hypertensives. BULL ENVIRON CONTAM TOXICOL 1984 May;32(5):525-32.

Mehta BC. Effects of iron deficiency — an iceberg phenomenon. J ASSOC PHYSICIANS INDIA 1984 Oct;32(10):895-900.

Milman N, Cohn J. Serum iron, serum transferrin and transferrin saturation in healthy children without iron deficiency. EUR J PEDIATR 1984 Dec;143(2):96-8.

Milman N, Cohn J, Pedersen NS. Serum ferritin and iron status of children in the Faroe Islands. EUR J PEDIATR 1984 Jun;142(2):89-92.

*Abstracted

*Mitchell DG, Doran D. Effect of bias in hematofluorometer measurements of protoporphyrin in screening programs for lead poisoning. CLIN CHEM 1985 Mar;31(3):386-90.

*Moller B, Carlsson LE, Johansson GI, Malmqvist KG, Hammarstrom L, Berlin M. Lead levels determined in Swedish permanent teeth by particle-induced X-ray emission. SCAND J WORK ENVIRON HEALTH 1982 Dec;8(4):267-72.

*Moreb J, Popovtzer MM, Friedlaender MM, Konijn AM, Hershko C. Evaluation of iron status in patients on chronic hemodialysis: relative usefulness of bone marrow hemosiderin, serum ferritin, transferrin saturation, mean corpuscular volume and red cell protoporphyrin. NEPHRON 1983;35(3):196-200.

Muys T. Quantitative determination of lead and cadmium in foods by programmed dry ashing and atomic-absorption spectrophotometry with electrothermal atomisation. ANALYST 1984 Feb;109(2):119-21.

*Okamoto Y, Kawai M. An association between increased porphyrin precursors and onset of abdominal symptoms in lead poisoning. TOXICOL LETT 1984 May;21(2):219-23.

Omenetto N, Human HG, Cavalli P, Rossi G. Direct determination of lead in blood by laser-excited flame atomic-fluorescence spectrometry. ANALYST 1984 Aug;109(8):1067-70.

Orssaud G, Claude JR, Moreau T, Lellouch J, Juguet B, Festy B. Blood lead concentration and blood pressure [letter]. BR MED J [Clin Res] 1985 Jan 19;290(6463):244.

Peter F, Bourdeau J. Screening for undue lead absorption: correlation between lead and erythrocyte protoporphyrin. CAN J PUBLIC HEALTH 1983 Sep-Oct;74(5):356-9.

Pleban PA, Mei DS. Trace elements in human seminal plasma and spermatozoa. CLIN CHIM ACTA 1983 Sep 15;133(1):43-50.

*Pocock SJ, Shaper AG, Ashby D, Delves T, Whitehead TP. Blood lead concentration, blood pressure, and renal function. BR MED J [Clin Res] 1984 Oct 6;289(6449):872-4.

Pollitt E, Soemantri AG, Yunis F, Scrimshaw NS. Cognitive effects of iron-deficiency anaemia [letter]. LANCET 1985 Jan 19;1(8421):158.

Pootrakul P, Wattanasaree J, Anuwatanakulchai M, Wasi P. Increased red blood cell protoporphyrin in thalassemia: a result of relative iron deficiency. AM J CLIN PATHOL 1984 Sep;82(3):289-93.

Prescott CW. Clinical findings in dogs and cats with lead poisoning. AUST VET J 1983 Sep;60(9):270-1.

*Raasch FO, Rosenberg JH, Abraham JL. Lead poisoning from hair spray ingestion. AM J FORENSIC MED PATHOL 1983 Jun;4(2):159-64.

Raftos J, Schuller M, Lovric VA. Iron stores assessed in blood donors by hematofluorometry. TRANSFUSION 1983 May-Jun;23(3):226-8.

*Reeves JD, Vichinsky E, Addiego J Jr, Lubin BH. Iron deficiency in health and disease. ADV PEDIATR 1983;30:281-320.

*Reeves JD, Yip R, Kiley VA, Dallman PR. Iron deficiency in infants: the influence of mild antecedent infection. J PEDIATR 1984 Dec;105(6):874-9.

Reizenstein P, Ljunggren G, Drougge E. Quality of diagnoses and cost of managing anemia in four countries. BIOMED PHARMACOTHER 1984;38(4):194-8.

Ridthmat W, Tantiniti P, Pathmasiriwat P, Choopanya K. Ascorbic acid in iron-deficiency anemia. J MED ASSOC THAI 1983 Dec;66(12):775-8.

*Roberts HJ. Potential toxicity due to dolomite and bonemeal. SOUTH MED J 1983 May;76(5):556-9.

*Rose DN, Cummings CE, Molinaro J, Fertig A. Screening for lead toxicity among autobody repair workers. AM J IND MED 1982;3(4):405-12.

*Rosen I, Wildt K, Gullberg B, Berlin M. Neurophysiological effects of lead exposure. SCAND J WORK ENVIRON HEALTH 1983 Oct;9(5):431-41.

Ruhr LP. Blood lead, δ-aminolevulinic acid dehydratase and free erythrocyte porphyrins in normal cattle. VET HUM TOXICOL 1984 Apr;26(2):105-7.

*Saenger P, Markowitz ME, Rosen JF. Depressed excretion of 6 β-hydroxycortisol in lead-toxic children. J CLIN ENDOCRINOL METAB 1984 Feb;58(2):363-7.

*Saltman P. Trace elements and blood pressure. ANN INTERN MED 1983 May;98(5 Pt 2):823-7.

*Saltzman BE, Yeager DW, Meiners BG. Reproducibility and quality control in the analysis of biological samples for lead and mercury. AM IND HYG ASSOC J 1983 Apr;44(4):263-7.

Sansone G, Ivaldi GD. Periodic-acid-Schiff positivity in erythroblasts of children with iron-deficiency anemia. PATHOLOGICA 1983 Sep-Oct;75(1039):681-5.

*Satzger RD, Bonnin E, Fricke FL. Development of a quality assurance program for determination of ultratrace background levels of lead and cadmium in raw agricultural crops by differential pulse anodic stripping voltammetry. J ASSOC OFF ANAL CHEM 1984 Nov-Dec;67(6):1138-40.

*Satzger RD, Kuennen RW, Fricke FL. Determination of lead in bonemeal by differential pulse anodic stripping voltammetry using a hydrochloric acid solubilization. J ASSOC OFF ANAL CHEM 1983 Jul;66(4):985-8.

*Abstracted

*Schottenfeld RS, Cullen MR. Organic affective illness associated with lead intoxication. AM J PSYCHIATRY 1984 Nov;141(11):1423-6.

Sensirivatana R, Supachadhiwong O, Phancharoen S, Mitrakul C. Neonatal lead poisoning. An unusual clinical manifestation. CLIN PEDIATR (Phila) 1983 Aug;22(8):582-4.

*Seppalainen AM. Electrophysiological evaluation of central and peripheral neural effects of lead exposure. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):43-52.

Serra TM, Serrano JF. Influence of phosphorus and calcium on flame atomic absorption spectrophotometric determination of lead in canned fish products. J ASSOC OFF ANAL CHEM 1984 Jan-Feb;67(1):186-7.

*Shamberger RJ. Effects of blood and urine on lead analyzed by flameless atomic absorption. J CLIN CHEM CLIN BIOCHEM 1983 Feb;21(2):107-11.

*Shapiro MD, Linas SL. Sodium chloride pica secondary to iron-deficiency anemia. AM J KIDNEY DIS 1985 Jan;5(1):67-8.

Shimayama T, Ono J, Katsuki T. Iron deficiency anemia caused by a giant jejunal diverticulum. JPN J SURG 1984 Mar;14(2):146-9.

*Shrivastava AK, Tandon SG. Studies on lead pollution: atomic absorption spectrophotometric determination of lead in hair and teeth samples. INT J ENVIRON ANAL CHEM 1984;17(3-4):293-8.

*Siegers CP, Jungblut JR, Klink F, Oberheuser F. Effect of smoking on cadmium and lead concentrations in human amniotic fluid. TOXICOL LETT 1983 Dec;19(3):327-31.

*Sinclair DF, Dohnt BR. Sampling and analysis techniques used in a blood lead survey of 1,241 children in Port Pirie, South Australia. CLIN CHEM 1984 Oct;30(10):1616-9.

*Singer R, Valciukas JA, Lilis R. Lead exposure and nerve conduction velocity: the differential time course of sensory and motor nerve effects. NEUROTOXICOLOGY (Park Forest Il) 1983 Summer;4(2):193-202.

Soemantri AG, Sudigbia I, Widjaya. Iron deficiency anemia among Indonesian children. PAEDIATR INDONES 1984 Jan-Feb;24(1-2):28-42.

*Speich M. Concentrations of lead, cadmium, and zinc in human heart muscle and aorta after acute myocardial infarction. J AM COLL NUTR 1982;1(3):255-62.

Stanwell-Smith R, Thompson SG, Haines AP, Ward RJ, Cashmore G, Stedronska J, Hendry WF. A comparative study of zinc, copper, cadmium, and lead levels in fertile and infertile men. FERTIL STERIL 1983 Nov;40(5):670-7.

Steinberg D. Anemia. A clinical perspective. CLIN BIOCHEM 1984 Apr;17(2):89-94.

*Sthapit PR, Ottaway JM, Fell GS. Determination of lead in blood by flame atomic-fluorescence spectrometry. ANALYST 1983 Feb;108(1283):235-43.

*Stober T, Stelte W, Kunze K. Lead concentrations in blood, plasma, erythrocytes, and cerebrospinal fluid in amyotrophic lateral sclerosis. J NEUROL SCI 1983 Sep;61(1):21-6.

*Subramanian KS, Meranger JC. Blood levels of cadmium, copper, lead and zinc in children in a British Columbia community. SCI TOTAL ENVIRON 1983 Sep;30:231-44.

*Subramanian KS, Meranger JC, Connor J. The effect of container material, storage time and temperature on cadmium and lead levels in heparinized human whole blood. J ANAL TOXICOL 1983 Jan-Feb;7(1):15-9.

*Subramanian KS, Meranger JC, MacKeen JE. Graphite furnace atomic absorption spectrometry with matrix modification for determination of cadmium and lead in human urine. ANAL CHEM 1983 Jun;55(7):1064-7.

Suga RS, Fischinger AJ, Koch FW, Noren I, Wallinder H, Lerner R. Determination of zinc protoporphyrin in blood [letter]. AM IND HYG ASSOC J 1983 May;44(5):B18-9.

Suma'mur PK, Heryuni S. Relationship of blood lead and manganese in occupationally unexposed subjects. ARH HIG RADA TOKSIKOL 1984 Jun;35(2):169-72.

*Taylor YP. Innovative modifications to the Delves cup blood-lead analysis procedure. AM IND HYG ASSOC J 1984 Dec;45(12):B12, B14, B16.

*Telisman S, Prpic-Majic D, Beritic T. PbB and ALAD in mentally retarded and normal children. INT ARCH OCCUP ENVIRON HEALTH 1983;52(4):361-9.

Thatcher RW, McAlaster R, Lester ML. Evoked potentials related to hair cadmium and lead in children. ANN NY ACAD SCI 1984;425:384-90.

Trimmer LM. Lead poisoning — a continuing adversary. EAR NOSE THROAT J 1983 Mar;62(3):136-41.

*Turlakiewicz Z, Jakubowski M, Chmielnicka J. Determination of diethyllead in the urine by flameless atomic absorption spectrometry. BR J IND MED 1985 Jan;42(1):63-6.

*Van der Weyden MB, Fong H, Hallam LJ, Breidahl MJ. Basic ferritin content of red cells of patients with anemia and polycythemia vera. PATHOLOGY 1984 Oct;16(4):419-23.

Van de Vyver FL, Vanheule AO, Verbueken AH, D'Haese P, Visser WJ, Bogaert W, et al. Patterns of iron storage in patients with severe renal failure. CONTRIB NEPHROL 1984;38:153-66.

van Oost BA, van den Beld B, Cloin LG, Marx JJ. Measurement of ferritin in serum: application in diagnostic use. CLIN BIOCHEM 1984 Aug;17(4):263-9.

*Abstracted

Waskerwitz MJ. Iron deficiency anemia in children. ISSUES COMPR PEDIATR NURS 1983 Sep-Dec;6(5-6):283-94.

Webster J, Wood A. Evaluation of an electrothermal atomisation procedure for the determination of lead in potable water. ANALYST 1984 Oct;109(10):1255-8.

Wedeen RP. Blood lead levels, dietary calcium, and hypertension [editorial]. ANN INTERN MED 1985 Mar;102(3):403-4.

Wedeen RP. Occupational renal disease. AM J KIDNEY DIS 1984 Jan;3(4):241-57.

*Wedeen RP, Batuman V, Landy E. The safety of the EDTA lead-mobilization test. ENVIRON RES 1983 Feb;30(1):58-62.

*Wielopolski L, Rosen JF, Slatkin DN, Vartsky D, Ellis KJ, Cohn SH. Feasibility of noninvasive analysis of lead in the human tibia by soft x-ray fluorescence. MED PHYS 1983 Mar-Apr;10(2):248-51.

Williams MK, Walford J, King E. Blood lead and the symptoms of lead absorption. BR J IND MED 1983 Aug;40(3):285-92.

Wong HB. The child with pallor. J SINGAPORE PAEDIATR SOC 1984;26(1-2):30-4.

*Wright LF, Saylor RP, Cecere FA. Occult lead intoxication in patients with gout and kidney disease. J RHEUMATOL 1984 Aug;11(4):517-20.

*Yip R, Dallman PR. Developmental changes in erythrocyte protoporphyrin: roles of iron deficiency and lead toxicity. J PEDIATR 1984 May;104(5):710-3.

Yip R, Johnson C, Dallman PR. Age-related changes in laboratory values used in the diagnosis of anemia and iron deficiency. AM J CLIN NUTR 1984 Mar;39(3):427-36.

Yip R, Schwartz S, Deinard AS. Hematocrit values in white, black, and American Indian children with comparable iron status. Evidence to support uniform diagnostic criteria for anemia among all races. AM J DIS CHILD 1984 Sep;138(9):824-7.

*Yip R, Schwartz S, Deinard AS. Screening for iron deficiency with the erythrocyte protoporphyrin test. PEDIATRICS 1983 Aug;72(2):214-9.

Zago MA, Costa FF, Bottura C. Dyserythropoiesis in iron deficiency and in β-thalassemia. BRAZ J MED BIOL RES 1984;17(2):135-42.

*Zink EW, Davis PH, Griffin RM, Matson WR, Moffitt RA, Sakai DT. Direct determination of lead in evaporated milk and apple juice by anodic stripping voltammetry: collaborative study. J ASSOC OFF ANAL CHEM 1983 Nov;66(6):1414-20.

*Zink EW, Moffitt RA, Matson WR. Rapid direct determination of lead in evaporated milk by anodic stripping voltammetry without sample pretreatment. J ASSOC OFF ANAL CHEM 1983 Nov;66(6):1409-13.

*Abstracted

EPIDEMIOLOGY

Chronological Trend in Blood Lead Levels Between 1976 and 1980

J.L. Annest, J.L. Pirkle, D. Makuc, J.W. Neese, D.D. Bayse, and M.G. Kovar. N ENGL J MED 1983 Jun 9;308(23):1373-7.

Authors' abstract: Analysis of a chronological trend in data from the second National Health and Nutrition Examination Survey indicated that average blood lead levels in the United States dropped approximately 37% (5.4 μg/dl) from February 1976 through February 1980. There was no evidence that this trend was due to errors in laboratory measurement or to the design of the survey. The trend was present even after accounting for differences in race, sex, age, region of the country, season, income, and degree of urbanization. Changes in exposure to lead in paint or in the diet are unlikely explanations of the trend. However, the correlation of blood lead levels with the lead level in gasoline was highly significant ($P < 0.001$) overall and in population subgroups defined by race, sex, and age. Although strong correlation does not prove cause and effect, the most likely explanation for the fall in blood lead levels is a reduction in the lead content of gasoline during this period.

Levels of Cadmium and Lead in Blood in Relation to Smoking, Sex, Occupation,and Other Factors in an Adult Population of the FRG

A. Brockhaus, I. Freier, U. Ewers, E. Jermann, and R. Dolgner. INT ARCH OCCUP ENVIRON HEALTH 1983;52(2):167-75.

Authors' abstract: Levels of cadmium (CdB) and lead (PbB) were determined in the blood of 579 60- to 65-year-old residents of Cologne and two small cities near Cologne. CdB levels in cigarette smokers are on the average 3-4 times higher than in nonsmokers (geometric means: nonsmokers, 0.44 μg/l; ≤ 10 cigarettes/d, 1.16 μg/l; > 10 cigarettes/d, 1.85 μg/l). The results indicate that, with regard to the internal dose, cadmium exposure via smoking may contribute even more than does exposure via food. PbB levels (geometric mean: 8.49 μg/100 ml; range: 2.9-30.3 μg/100 ml) are in the acceptable range as defined by the Commission of the European Communities (CEC) reference values. Male smokers have on the average slightly higher PbB levels than male nonsmokers. In women PbB levels are on the average lower than in men.

Changes in Blood Lead Concentrations in Women in Wales 1972-82

P.C. Elwood. BR MED J [CLIN RES] 1983 May 14;286(6377):1553-5.

Author's abstract: Blood lead concentrations, estimated in epidemiological surveys of adult women in Wales, have shown a fall of over 30% since 1972. During the same period the amount of lead in petrol has changed little, but general traffic flow has steadily increased; there has been no change in the amount of lead in water.

Assessment of Exposure to Lead and Cadmium Through Biological Monitoring: Results of a UNEP/WHO Global Study

L. Friberg and M. Vahter. ENVIRON RES 1983 Feb;30(1):95-128.

Authors' abstract: This paper describes a United Nations Environment Program/World Health Organization (UNEP/WHO) project on the assessment of human exposure to lead and cadmium through analysis of blood and kidneys. The following countries have participated: Belgium, India, Israel, Japan, Mexico, People's Republic of China, Peru, Sweden, United States, and Yugoslavia. No laboratory started the monitoring before achieving satisfactory results of quality control (QC) analysis (samples of cow blood spiked with lead and cadmium and freeze-dried horse kidney cortex for cadmium analysis) according to predetermined criteria based on a linear regression model. Two hundred teachers from one urban area in each country constituted the target group for lead and cadmium in blood and cases of "sudden, unexpected death" for cadmium in kidney cortex. QC samples were analyzed in parallel with the monitoring samples to assure validity of the obtained results. The quality assurance program also included preanalytical quality control. There was considerable variation in metal exposure between areas. Geometric means for lead in blood ranged from about 60 μg Pb/liter in Beijing and Tokyo to 225 in Mexico City. The values also were below 100 μg Pb/liter in Baltimore, Jerusalem, Lima, Stockholm, and Zagreb, and between 100 and 200 μg Pb/liter in Brussels and India. In general, males had higher blood levels than females and smokers had higher levels than nonsmokers. With a few exceptions, the values were lower than results reported in a recent study within the European Communities. Geo-

metric means for cadmium in blood ranged from 0.5 μg Cd/liter in Stockholm and Jerusalem to 1.2 in Brussels and Tokyo. Cadmium levels were considerably higher among smokers than among nonsmokers. Tokyo had the highest values for cadmium in kidney cortex, with a geometric mean in the age group 40-60 years of 60-70 mg Cd/kg wet wt. Lowest values were found in Baltimore, Beijing, India, and Jerusalem, with means around 20-25 mg Cd/kg wet wt. There was a tendency toward higher values for smokers than for nonsmokers, but no differences were related to sex. Data were not received from Mexico and Peru.

Blood Lead and Blood Pressure. Relationship in the Adolescent and Adult U.S. Population

W.R. Harlan, J.R. Landis, R.L. Schmouder, N.G. Goldstein, and L.C. Harlan. JAMA 1985 Jan 25;253(4):530-4.

Authors' abstract: Heavy lead exposure has been connected to cardiovascular disease, but modest exposures encountered in the general environment have not been associated previously with disease risk. The relationship between blood lead levels and blood pressures was examined by using data from the second National Health and Nutrition Examination Survey. A direct relationship was found between blood lead levels and systolic and diastolic pressures for men and women and for white and black persons aged 12 to 74 years. Blood lead levels were significantly higher in younger men and women (aged 21 to 55 years) with high blood pressure, but not in older men or women (aged 56 to 74 years). In multiple regression analyses, the relationship of blood lead to blood pressure was independent of other variables for men, but not for women. Dietary calcium and serum zinc levels were inversely related to blood pressure.

A Prospective Study on Early Neurotoxic Effects of Lead

S. Hernberg, A.M. Seppalainen, and P. Mantere. ANN ACAD MED SINGAPORE 1984 Apr; 13 (2 Suppl): 378-82.

Authors' abstract: A prospective follow-up study on new lead workers who entered a storage battery factory was carried out between 1975 and 1981. Nerve conduction velocities and psychological performance were recorded before the commencement of exposure and after 1, 2, and 4 years of work, respectively. Out of an initial number of 89 workers, 23 were available for the 1-year, 16 for the 2-year, and 11 for the 4-year reexamination. The reference group comprised nonexposed workers of a cable manufacturing plant and an electrical power plant. In particular, the sensory conduction velocities of the median nerve decreased during the 2-year follow-up. When divided into two groups according to the median Pb-B values (27-30 μg/100 ml), the higher exposure group showed slower values for several motor and sensory conduction velocities at the 1- and 2-year examination as compared with the lower group. Further, visual intelligence and visuomotor functions had impaired significantly. The learning effect for some psychological tests, which was clearly evident among the referents, was almost absent among the lead workers. After 4 years, only 11 lead workers remained. This, together with selection in the drop-out group, resulted in the group differences found for conduction velocities and psychological tests not reaching statistical significance.

Epidemiology, Etiology, and Prevention of Multiple Sclerosis. Hypothesis and Fact

T.H. Ingalls. AM J FORENSIC MED PATHOL 1983 Mar;4(1):55-61.

Author's abstract: Slow, retrograde seepage of ionic mercury from root canal or Class V amalgam fillings inserted many years previously, recurrent caries and corrosion around filling edges, and the oxidizing effect of the purulent response may lead to multiple sclerosis (MS) in middle age. Epidemiologic studies of MS consistently reveal more neurological disease in the North, inferentially because there may be fewer caries and therefore fewer fillings done in the South. Clinical and epidemiologic data also suggest that a second heavy metal, lead, may operate almost interchangeably with mercury. Possibly, cases of unilateral MS derive from mercury-amalgam fillings in ipsolateral teeth, whereas the generalized disease may result from ingestion or inhalation of volatile mercury or exhaust fumes of lead additives to gasoline. The forensic and preventive medical challenge is to identify, monitor, and resolve questions of hidden heavy metal hazards in a high technology society, especially those of lead and mercury. Further clinical-epidemiologic and basic science studies of heavy metal assays in whole blood, CNS [central nervous system] tissues, packed cells, and serum are warranted. Prevention awaits further testing of the hypothesis and experience with substitute filling materials.

Epidemiologic Study of Renal Function in Copper Smelter Workers

R. Lilis, J.A. Valciukas, J.P. Weber, J. Malkin, and I.J. Selikoff. ENVIRON HEALTH PERSPECT 1984 Mar;54:181-9.

Authors' abstract: A medical cross-sectional examination of a copper smelter work force was undertaken after environmental contamination with lead, cadmium, and arsenic had been documented. A total of 920 subjects were examined, including active smelter employees,

retired workers, and copper mine employees who had never worked in the smelter. Slight to moderate absorption of lead and cadmium was definitely present in the active copper smelter employees, who had significantly higher levels of blood lead (Pb-B), zinc protoporphyrin (ZPP), and blood cadmium (Cd-B) than retired employees and miners. Urinary cadmium (Cd-U) levels were higher in retired workers, who were also older and had, as a group, longer duration of exposure in the smelter. Cd-U did not exceed 10 μg/g creatinine, the level considered critical for nephrotoxicity, in any of the subjects. Median Cd-B level for active workers was 2.75 μg/L. Lead absorption was characterized by a relatively small proportion (16.7%) of active employees with Pb-B levels 40 μg/dL or higher. We were particularly interested in exploring the possibility that simultaneous exposure to lead and cadmium, although at levels not associated with nephrotoxicity for each metal separately, could result in renal function impairment. Distribution patterns of BUN and serum creatinine levels were unremarkable. Urinary β-2-microglobulin levels were less than 200 μg/g creatinine in 95% of copper smelter employees. There were no significant correlations between urinary β-2-microglobulin levels and Cd-U, Cd-B, Pb-B, and ZPP or between urinary β-2-microglobulin excretion and serum creatinine or BUN levels. Urinary β-2-microglobulin levels were significantly correlated with age in the copper smelter workers, but not in the miners. Nevertheless, in the absence of any significant correlations between urinary β-2-microglobulin and Cd-U and Cd-B, a causal relationship with cadmium absorption cannot be affirmed. That kidney function could be impaired by long-term exposure in the smelter was only indirectly suggested. Effects on renal function at the low levels of cadmium and lead absorption that were observed in this smelter population are minimal.

Health Effects of Low Level Occupational Exposure to Lead: The Trail, British Columbia Study

L.C. Neri, H. Johansen, and D. Hewitt. ARCH ENVIRON HEALTH 1983 May-Jun;38(3):180-9.

Authors' abstract: Blood lead (PbB) was measured in a sample of 245 lead smelter employees and their wives in Trail, B.C., and 144 controls in Nelson, B.C. Smelter workers were divided into three groups according to lead exposure: (1) directly-exposed, (2) indirectly-exposed, and (3) office workers. The average PbB values found (41, 33, and 16 μg/dl, respectively) reflected exposure level. In the highest exposure group, male smokers had significantly higher PbB concentrations than nonsmokers (44 vs. 37 μg/dl). For exposed males, average number of "days off work ill" increased with increasing PbB range, and significant correlations were found between PbB values and five biologically plausible health symptoms. None of those symptoms planted to detect response bias correlated. Because of a 4-month strike, PbB values were measured in a subsample from each exposure group before and 1, 2, and 4 months after smelter operation resumed. Exposed workers' PbB levels stabilized after 1 month's operation.

Lead Levels in Whole Blood of an Adult Population Group from Rome

G. Pallotti, A. Consolino, B. Bencivenga, V. Iacoponi, G. Morisi,and F. Taggi. SCI TOTAL ENVIRON 1983 Oct;31(1):81-7.

Authors' abstract: Pb-blood levels of 801 adult nonoccupationally exposed subjects from Rome are reported. The investigation was carried out according to EEC [European Economic Community] Directive No. 77/312 with acceptable quality control of analytical data. A mean Pb-blood level of 173 μg/l (198 μg/l for males and 150 μg/l for females) was found; good correlations were found between Pb-blood levels and age, sex, and smoking habits, but no correlation was found in relation to drinking habits, residence, and other variables that were examined. In the present survey all the three EEC reference levels were observed.

Effects of Tap Water Lead, Water Hardness, Alcohol, and Cigarettes on Blood Lead Concentrations

S.J. Pocock, A.G. Shaper, M. Walker, C.J. Wale, B. Clayton, T. Delves, R.F. Lacey, R.F. Packham, and P. Powell. J EPIDEMIOL COMMUNITY HEALTH 1983 Mar;37(1):1-7.

Authors' abstract: A survey of middle-aged men in 24 British towns has found pronounced geographical variation in blood lead concentrations. Towns with the highest mean blood lead concentrations have soft water supplies and have the highest water lead concentrations. Individual blood lead can be considerably increased by raised household tap water lead concentrations. Mean blood lead is estimated to be 43% higher for men when the concentration of lead in first-draw domestic tap water is 100 μg/l compared with a zero concentration. Individual blood lead is also affected by alcohol consumption and cigarette smoking, such that on average these two lifestyle habits together contribute an estimated 17% to the blood concentration of lead in middle-aged men. Lead in water should be given greater priority in any national campaign to reduce lead exposure.

Urinary Cadmium and Lead Concentrations and Their Relation to Blood Pressure in a Population with Low Exposure

J. Staessen, C.J. Bulpitt, H. Roels, A. Bernard, R. Fagard, J.V. Joossens, R. Lauwerys, P. Lijnen, and A. Amery. BR J IND MED 1984 May;41(2):241-8.

Authors' abstract: The 24-hour urinary excretion of cadmium (U-Cd) and lead (U-Pb) and the excretion of β-2-microglobulins and retinol-binding protein concentration in spot urines were determined in a random 4% sample of the population of a small Belgian town. Blood pressure and body weight were measured on two separate occasions. U-Cd averaged 2.4 nmol/24 h in 46 youths, increased with age, and was significantly higher in 57 adult men as compared with 59 women (9.3 versus 7.2 nmol/24 h; $p < 0.01$). U-Pb averaged 28 nmol/24 h in youths and similarly increased with age: adult men excreted more lead than women (64 versus 40.0 nmol/24 h; $p < 0.001$). Among men, manual workers excreted more cadmium (12.6 versus 7.5 nmol/24 h; $p < 0.05$) but a similar amount of lead (62 versus 61 nmol/24 h) compared with office workers. After sex and age were adjusted for, U-Cd and U-Pb were not related to body weight and cigarette consumption. In simple regression analysis, U-Cd was positively correlated with both systolic ($r = +0.30$; $p < 0.05$) and diastolic ($r = +0.38$; $p < 0.01$) blood pressure in women. After other contributing variables were adjusted for, however, a weak but negative relation became apparent between systolic pressure and U-Cd in women ($t = -2.21$; $p = 0.033$) and between diastolic pressure and U-Cd in men ($t = -2.04$; $p = 0.047$).

Occupational Exposures Among Fathers of Children with Wilms' Tumor

J.R. Wilkins, 3d and T.H. Sinks, Jr. J OCCUP MED 1984 Jun;26(6):427-35.

Authors' abstract: An occupation-and-exposure linkage system was utilized to perform an epidemiologic case-control study of paternal occupation and Wilms' tumor in offspring. The first part of the study was designed to test the hypothesis that paternal lead (Pb) exposure is a risk factor for Wilms' tumor in offspring. The second part of the study was an exploratory analysis that sought to generate possible etiologic hypotheses about other paternal exposures in the workplace in relation to Wilms' tumor. Calculation of odds ratios indicated that there was no statistical difference in the frequency of occupational exposure to Pb, Pb alkyls, and Pb salts for fathers of children with Wilms' tumor and fathers of controls, a finding that contrasts sharply with the results of the one previously reported study in this area. In the exploratory phase of the study, case fathers were found more likely to have been exposed to boron, whereas control fathers were found more likely to have encountered insecticides, acetylene, o-chlorobenzylidene, oil orange ss, and diethylene glycol; the differences were statistically significant. Troublesome methodologic problems, including exposure misclassification, sample size, and multiple comparisons, are discussed.

Epidemiological Monitoring of Environmental Lead Exposures in California State Hospitals

Y. Yaffe, D. Jenkins, H. Mahon-Haft, W. Winkelstein, C.P. Flessel, and J.J. Wesolowski. SCI TOTAL ENVIRON 1984 Jan 27;32(3):261-75.

Authors' abstract: Blood lead screening of 8,062 state hospital residents in California revealed 143 residents with excessive lead levels (≥ 30 μg/dL). This screening was part of the Childhood Lead Project and was performed in 1978. The purpose of this study was to identify "critical" lead sources in California state hospitals. Accurate identification is crucial if subsequent abatement programs are to be effective. The strategy involved the following sequence of steps: 1) selecting cases on the basis of blood lead and erythrocyte protoporphyrin screening; 2) determining pica habits and environmental exposures through interviews with ward's staff and/or parents; 3) measuring lead levels in environmental samples reflecting exposures; 4) interpreting these data in order to identify critical lead sources; 5) reducing exposure to critical lead sources; and 6) following up of cases and controls to validate the effects of this strategy. A group of 36 lead-burdened cases with pica (30-60 μg Pb/dL blood) and 36 matched controls (PbB < 20 μg/dL) were selected from among the developmentally disabled residents of two California state hospitals. These subjects were studied in order to identify the lead sources to which they were exposed and to abate the major ones. Three major lead sources were found in the state hospitals: wall and furniture paints (100-45,400 μg Pb/g paint) and surface soil (33-570 μg Pb/g soil). An educational format was presented to all involved staff. The results have indicated a trend towards lower lead intake by the lead-burdened cases. In one of the two hospitals a "lead-free unit" had been established. All the lead-burdened cases were transferred to this unit in August 1981. A few months later the blood lead levels of all the cases dropped below 30 μg/dL. Initial epidemiological monitoring indicated where there were preventable hazards, which abatement efforts succeeded in reducing. Further monitoring of such problems is indicated in this and other developmentally disabled populations.

SELECTED BIBLIOGRAPHY

*Annest JL, Pirkle JL, Makuc D, Neese JW, Bayse DD, Kovar MG. Chronological trend in blood lead levels between 1976 and 1980. N ENGL J MED 1983 Jun 9;308(23):1373-7.

Anonymous. Blood lead levels for persons ages 6 months — 74 years: United States, 1976-80. VITAL HEALTH STAT [11] 1984 Aug;11(233):1-59.

*Brockhaus A, Freier I, Ewers U, Jermann E, Dolgner R. Levels of cadmium and lead in blood in relation to smoking, sex, occupation, and other factors in an adult population of the FRG. INT ARCH OCCUP ENVIRON HEALTH 1983;52(2):167-75.

*Elwood PC. Changes in blood lead concentrations in women in Wales 1972-82. BR MED J [CLIN RES] 1983 May 14;286(6377):1553-5.

*Friberg L, Vahter M. Assessment of exposure to lead and cadmium through biological monitoring: results of a UNEP/WHO global study. ENVIRON RES 1983 Feb;30(1):95-128.

*Harlan WR, Landis JR, Schmouder RL, Goldstein NG, Harlan LC. Blood lead and blood pressure. Relationship in the adolescent and adult U.S. population. JAMA 1985 Jan 25;253(4):530-4.

*Hernberg S, Seppalainen AM, Mantere P. A prospective study on early neurotoxic effects of lead. ANN ACAD MED SINGAPORE 1984 Apr;13(2 Suppl):378-82.

*Ingalls TH. Epidemiology, etiology, and prevention of multiple sclerosis. Hypothesis and fact. AM J FORENSIC MED PATHOL 1983 Mar;4(1):55-61.

Landrigan PJ, Baker EL Jr. Epidemiological aspects of occupational lead poisoning. SANGYO IKA DAIGAKU ZASSHI 1983 Mar 20;5 Suppl:145-55.

*Lilis R, Valciukas JA, Weber JP, Malkin J, Selikoff IJ. Epidemiologic study of renal function in copper smelter workers. ENVIRON HEALTH PERSPECT 1984 Mar;54:181-92.

Murphy RS. A role for National Health and Nutrition Examination Surveys in exposure assessment. J TOXICOL CLIN TOXICOL 1983-84;21(1-2):299-320.

*Neri LC, Johansen H, Hewitt D. Health effects of low level occupational exposure to lead: the Trail, British Columbia study. ARCH ENVIRON HEALTH 1983 May-Jun;38(3):180-9.

*Pallotti G, Consolino A, Bencivenga B, Iacoponi V, Morisi G, Taggi F. Lead levels in whole blood of an adult population group from Rome. SCI TOTAL ENVIRON 1983 Oct;31(1):81-7.

*Pocock SJ, Shaper AG, Walker M, Wale CJ, Clayton B, Delves T, Lacey RF, Packham RF, Powell P. Effects of tap water lead, water hardness, alcohol, and cigarettes on blood lead concentrations. J EPIDEMIOL COMMUNITY HEALTH 1983 Mar;37(1):1-7.

*Staessen J, Bulpitt CJ, Roels H, Bernard A, Fagard R, Joossens JV, Lauwerys R, Lijnen P, Amery A. Urinary cadmium and lead concentrations and their relation to blood pressure in a population with low exposure. BR J IND MED 1984 May;41(2):241-8.

*Wilkins JR 3d, Sinks TH Jr. Occupational exposures among fathers of children with Wilms' tumor. J OCCUP MED 1984 Jun;26(6):427-35.

*Yaffe Y, Jenkins D, Mahon-Haft H, Winkelstein W, Flessel CP, Wesolowski JJ. Epidemiological monitoring of environmental lead exposures in California State Hospitals. SCI TOTAL ENVIRON 1984 Jan 27;32(3):261-75.

*Abstracted

Development and Plasticity of the Hippocampal-Cholinergic System in Normal and Early Lead Exposed Rats

D.P. Alfano, T.L. Petit, and J.C. LeBoutillier. BRAIN RES 1983 Oct;312(1):117-24.

Authors' abstract: A review of previous evidence suggested the possibility of a functional association between the effects of early lead (Pb) exposure, hippocampal damage, and cholinergic deficiency. To further assess this possibility, we exposed Long-Evans hooded rat pups to Pb for the first 25 postnatal days via the maternal milk. Dams were fed either 4.0% $PbCO_3$ or a Na_2CO_3 control diet throughout this period. At 30 and 115 days of age, the brains of Pb and control animals were processed for acetylcholinesterase histochemistry. Morphometric evaluation of the molecular layer of the hippocampal dentate gyrus indicated that although absolute increases in the dimensions of the afferent systems to the hippocampal dentate gyrus are observed between 30 and 115 days of age, no significant rearrangement in the pattern of lamination occurs during this time. No effects of Pb were seen on the development of the cholinergic innervation of this brain region at either of these ages. Unilateral perforant path transections performed on Pb and control animals at 100 days of age indicated reduced cholinergic plasticity in the molecular layer of the hippocampal dentate gyrus of Pb-exposed animals, as indicated by acetylcholinesterase histochemistry. These findings indicate that a decrease in neuroanatomical plasticity may be a critical brain mechanism underlying the learning deficits observed following exposure to Pb.

Mechanism of Action of Lead on Neuromuscular Junctions

W.D. Atchison and T. Narahashi. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):267-82.

Authors' abstract: Effects of bath-applied lead acetate on nerve-evoked and spontaneous neurotransmitter release were studied at the neuromuscular junction of the rat by using conventional microelectrode recording techniques. Lead (20, 100 μM) depressed end-plate potential (EPP) amplitude within 5 min of application without affecting miniature end-plate potential (MEPP) amplitude. Increasing bath Ca^{2+} concentration from 2 mM to 4 or 8 mM caused a concentration-dependent reversal of lead-induced block of nerve-evoked EPPs. When lead was washed out of the bath, EPP amplitude either returned to control values or was potentiated. Mean quantal content (m) was reduced significantly by lead treatment, an effect due primarily to a decrease in the immediately available store of transmitter (n). The probability of transmitter release (p) was either unchanged or slightly increased by lead. In contrast to its depressant effect on evoked transmitter release, spontaneous transmitter release, as measured by MEPP frequency, was increased by lead. MEPP frequency was increased from control levels of 1.2-3.2/sec to 12-16/sec by 100 μM lead. When lead was removed from the bath solution, MEPP frequency returned to control levels. Lead-induced increases in MEPP frequency still occurred when Ca^{2+} was removed from the external bath solution or when 1 mM Mn^{2+} was added to block nerve terminal Ca^{2+} channels, suggesting that extracellular Ca^{2+} is not required for lead to increase spontaneous release. It is suggested that lead exerts actions at multiple sites at the presynaptic nerve terminal. An extracellular action of lead on transmitter release mechanisms is likely to be due to a competitive antagonism with Ca^{2+} for entry through Ca^{2+} channels. An intracellular action of lead is indicated by the depression of n and the ability of lead to stimulate spontaneous acetylcholine release in the absence of external Ca^{2+} entry.

Effects of Chronic Low Level Lead Exposure on the Physiology of Individually Identifiable Neurons

G. Audesirk and T. Audesirk. NEUROTOXICOLOGY (Park Forest Il) 1983 Winter;4(4):13-26.

Authors' abstract: Although chronic exposure to lead has been correlated with a variety of behavioral and neurochemical deficits in humans and other mammals, little is known of the mechanisms of action of chronic lead at the level of the individual nerve cell. We have used the individually identifiable neurons of the freshwater pond snail *Lymnaea stagnalis* as a model system for investigating the effects of chronic low-level (5 μM) lead exposure on neuronal physiology. Thirteen neuronal parameters were measured with intracellular microelectrode recording in each of six different identifiable neurons or homogeneous neuron clusters. Results were analyzed by a multivariate analysis of variance (MANOVA). MANOVA analysis indicates that there is a significant overall effect of lead exposure ($p = 0.0001$) and a

significant interaction between lead and neuron type ($p = 0.01$). In most neuron types, chronic lead causes an increase in the resting potential, a slowing of recovery of the membrane potential after the undershoot of a spike, a decrease in spontaneous spiking activity, and a decrease in the input resistance. Lead also has differential effects on identifiable neurons, depressing excitability in some neuron types while not altering excitability in others.

Inhibition of Oral Lead Absorption in Rats by Phosphate-Containing Products

B.J. Aungst and H.L. Fung. J PHARM SCI 1983 Apr;72(4):345-8.

Authors' abstract: Recent studies indicate that elevated blood lead levels in children are largely a result of exposure to this metal via the oral route. A logical approach to decrease or prevent lead intoxication would be to reduce its absorption as soon as lead ingestion is known or suspected. At present, however, there are no readily available products recommended to accomplish this goal. It was found that a phosphate-buffered, saline laxative reduced lead absorption over 50% in rats administered a single oral lead acetate dose, presumably by promoting the formation of less soluble lead salts. A popular phosphate-containing carbonated beverage also decreased lead absorption approximately 30% after oral lead acetate or lead-based paint doses, possibly by decreasing solubility, dissolution rate, and gastrointestinal motility. It is possible that these household products, and those with similar ingredients, may be safely used to reduce lead absorption in humans.

Lead Induced Alterations in Maternal Behavior and Offspring Development in the Rat

J. Barrett and P.J. Livesey. NEUROBEHAV TOXICOL TERATOL 1983 Sep-Oct;5(5):557-63.

Authors' abstract: The study was designed to determine whether lead ingestion by nursing rats would affect dam-pup interaction. Dams were exposed to diets with 0.0, 0.2, 0.4, or 1.0 percent by weight metallic lead. Mean blood-lead levels of pups at weaning were 3, 19, 40, and 57 μg/100 ml of blood, respectively. Maternal behavior was assessed by videotaping behavior for complete 24-hour periods on alternate days from birth to weaning. Analysis of data revealed that lead affected dams nursed for longer periods than normal and that offspring were slower to explore their environment. It was concluded that altered maternal behavior was related to delays in pup development and that the functional isolation of experimental pups from their environment may be the antecedent to altered behavior later in maturity.

The Effect of Clinical and Subclinical Concentrations of Lead on the In Vitro Aging of Human Fibroblasts

P. Bemiller and E.R. Kraus, Jr. MECH AGEING DEV 1983 May;22(1):79-87.

Authors' abstract: The effect of 20, 40, and 80 μg per 100 ml concentrations of lead on the in vitro senescence of fetal human diploid fibroblasts IMR-90 was determined. The areas and dry mass of the cell, nucleus, and nucleolus were measured at early, middle, and late passages. There was a decrease in total population doublings as the concentration of lead in the medium was increased. Although there was a decrease in the number of nucleoli per cell with successive doublings, there was no difference between controls and lead-treated cells. There was an increase in nucleolar dry mass as the cells aged, and this was most noticeable in the 40- and 80-μg groups. There were no noteworthy changes in nuclear and cellular areas and dry mass with respect to lead treatment. The results are discussed, and it is concluded that even subclinical concentrations of lead cause an acceleration of cellular aging in vitro.

Conversion of Inorganic Lead into a Highly-Toxic Organic Derivative by Marine Microorganisms

I. Berdicevsky, M. Shachar, and S. Yannai. ARCH TOXICOL [SUPPL] 1983;6:285-91.

Authors' abstract: It has been reported that certain microorganisms isolated from lake sediments may transform inorganic lead compounds to organic derivatives, which are by at least one order of magnitude more toxic than the parent (inorganic) compounds. The purpose of this study was to investigate whether microorganisms isolated from a marine sediment could also produce such metabolites in an in vitro system simulating the marine ecosystem. The experimental setup included: 1) A sterile control system containing added inorganic lead (referred to as Pb^{2+}); 2) a nonsterile control system without added Pb^{2+}; 3) a nonsterile experimental system containing added Pb^{2+}. The amount of added Pb^{2+} ranged from 5 to 1,000 ppm. Aliquots were taken at different intervals from the nonsterile systems, and the surviving microorganisms were identified and counted. The main results were as follows: 1) The higher lead levels were toxic to all microorganisms. 2) Organic lead was only detected in the nonsterile experimental system, apparently due to microbial action, since none was found in the sterile systems. 3) Several bacteria exhibiting various degrees of tolerance for lead were isolated.

Adsorption of Pu, Pb and Cd to Mouth Surfaces During Oral Administration to Mice

M.H. Bhattacharyya, R.P. Larsen, H.C. Furr, D.P. Peterson, R.D. Oldham, E.S. Moretti, and M.I. Spaletto. HEALTH PHYS 1985 Feb;48(2):207-13.

Authors' abstract: Substantial adsorption of Pu, Cd, and Pb onto mouth surfaces of mice occurs during consumption of drinking water that contains these elements. If this adsorption is not taken into account, the amounts deposited in the eviscerated carcass (muscle plus skeleton) after gastrointestinal absorption are overestimated by 2-9 times for the experiments described. An evaluation of data indicates that significant adsorption can also occur during gavage administration. Methods are described for estimation of amounts deposited in the carcass after exposure of mice to these metals via drinking water or gavage.

A Retrospective Study of Lead Poisoning in Cattle

B.R. Blakley. VET HUM TOXICOL 1984 Dec;26(6):505-7.

Author's abstract: Information pertaining to 294 cases of bovine lead poisoning that occurred during the 15-year period from 1968 to 1982 was collected from the toxicology laboratory records at the Western College of Veterinary Medicine. Lead poisoning was seen more often in younger cattle, with 51.9% of the cases reported in animals 6 months of age or less. A statistically significant seasonal incidence was seen ($p < 0.0001$), with 60.9% of the cases occurring from May to August. Lead poisoning was more common in dairy breeds than beef breeds. The relative rates in the dairy and beef breeds per 1,000 cattle were 0.022 and 0.0065, respectively. No specific breed susceptibility was associated with any of the major dairy or beef breeds. Statistically significant sex-related differences for lead poisoning were not seen ($p = 0.11$). The most suitable biological samples utilized to confirm lead poisoning were blood, kidney, and liver. These samples produced the most reliable results, with rumen and fecal samples exhibiting a high degree of variability.

Osteoclast Changes Induced by Lead Poisoning (Saturnism)

E. Bonucci, R.H. Barckhaus, G. Silvestrini, P. Ballanti, and G. Di Lorenzo. APPL PATHOL 1983;1(5):241-50.

Authors' abstract: In this paper we report the results of histological, histochemical, and electron microscopic investigations, and of electron probe analysis, carried out on bone cells of tibiae and femurs of lead-poisoned collie puppies. The most important changes were found in osteoclasts. They were increased in number, showed intranuclear and intracytoplasmic inclusion bodies, and frequently had shrunk, pyknotic nuclei and were detached from bone matrix. Organic components were histochemically demonstrable in the inclusion bodies, which consisted of a central core, peripheral filaments, and intrinsically electron-dense granules. Lead was detected in the inclusion bodies by electron probe elemental analysis: Pb-L α pulses in the regions with inclusions are four times higher than those in the cytoplasm. Osteoblasts and osteocytes did not contain inclusion bodies, probably because in them lead does not reach a concentration sufficiently high to induce inclusion formation. On the contrary, this concentration can be reached in the osteoclasts when, during bone resorption, they accumulate the lead salts previously incorporated in the bone matrix.

Neonatal Triethyl Lead Neurotoxicity in Rat Pups: Initial Behavioral Observations and Quantification

R.M. Booze, C.F. Mactutus, Z. Annau, and H.A. Tilson. NEUROBEHAV TOXICOL TERATOL 1983 May-Jun;5(3):367-75.

Authors' abstract: Although alterations in development due to inorganic lead poisoning have been intensely investigated, little is known about the early toxicity of organic lead compounds. Assessment of developmental consequences due to triethyl lead (TEL) intoxication included (1) determination of the acute LD_{50} as 13 ± 1 mg/kg and (2) detailed examination of early neurobehavioral sequelae. The offspring of 12 Fischer-344 dams were administered on postpartum day 5 either a sham-injection, 15% ethanol, 3 mg/kg or 6 mg/kg TEL via subcutaneous injection (20 μl). Small, but significant, weight reductions of 6% and 13% for the 3- and 6-mg/kg TEL-dosed pups, respectively, were observed (days 14-30). Early sensory deficits of TEL pups as indicated by impaired olfactory discrimination on day 7 and decreased incidence of nipple attachment on day 9 were accompanied by the presence of fine whole-body tremor (day 10). Although these initial effects were transitory in nature, activity evaluations demonstrated persistent hypoactivity in high-dose TEL males (days 15, 22, 24, 26, and 29). Passive avoidance acquisition was not affected by TEL treatment (day 18). However, 72- and 144-hr tests of passive avoidance retention (days 21 and 25) suggested alterations in affective behavior, i.e., hypoactivity in high-dose TEL males and hyperactivity in low-dose TEL females. A reduction in number, but not magnitude, of startle responses also occurred as a function of TEL exposure. The single postnatal day 5 injection of TEL thus produced transitory effects possibly reflecting direct TEL pharmacological activity, as well as apparent long-term effects suggesting potential permanent alterations in behavioral function.

Comparative Effects of Ca-Ethylenediaminetetraacetic Acid (EDTA), ZnEDTA, and ZnCaEDTA in Mobilizing Lead

C.F. Brownie and A.L. Aronson. TOXICOL APPL PHARMACOL 1984 Sep 15;75(2):167-72.

Authors' abstract: Male Long-Evans rats weighing approximately 240 g were given Pb at 14 mg/kg as the acetate by slow intravenous (iv) infusion 17 days before chelate treatment. The chelating agents were administered by continuous iv infusion at either 1 mmol/kg over 6 hr or 6 mmol/kg over 24 hr or at 0.16 mmol/kg/day by subcutaneous (sc) injections. ZnEDTA was 60% and ZnCaEDTA was 76% as effective as CaEDTA in promoting urinary Pb excretion at 1 mmol/kg over 6 hr, iv. At 6 mmol/kg/24 hr, iv, ZnEDTA was 76% and ZnCaEDTA was 98% as effective as CaEDTA. Mean urinary Pb excretion for each chelate via the sc route and the lowest iv route of administration was the same. Blood δ-aminolevulinic acid dehydratase (ALAD) activity (an indicator of Pb toxicity) was enhanced approximately twofold by CaEDTA, 2 1/2-fold by ZnCaEDTA, and fivefold by ZnEDTA treatment. It is suggested that the safety of EDTA can be markedly enhanced if administered as a ZnCaEDTA chelate without appreciably diminishing its efficacy in promoting urinary Pb excretion.

The Effects of Lead on the Developing Central Nervous System of the Rat

R.J. Bull, P.T. McCauley, D.H. Taylor, and K.M. Croften. NEUROTOXICOLOGY (Park Forest Il) 1983 Spring;4(1):1-17.

Authors' abstract: Biochemical and structural development of the cerebral cortex of rat pups is delayed by low levels of lead administered in the dam's drinking water during gestation and suckling periods. These changes in brain development coincide with delays in the development of exploratory and locomotor activity and impaired learning. Subsequent cross-fostering experiments have shown that delays in synaptogenesis and in the development of exploratory behavior were attributed entirely to the prenatal, as opposed to the postnatal, exposure to lead at the low dose levels utilized. Examination of the variations in blood lead concentrations in pups and dams during gestation and until weaning at 21 days of postnatal age indicated that a substantial increase in blood lead concentrations occurred late in pregnancy. At 200 mg of Pb/liter of drinking water, peak blood Pb concentrations were observed to be approximately 60 μg/dl in dams and 80 μg/dl in pups on the 20th day of gestation. By the 10th postnatal day blood Pb concentrations had decreased to 35 μg/dl in dams and 40 μg/dl in pups, despite an increased consumption of drinking water containing the same concentration of Pb during this period. (Delays in cerebral cortical development were observed after 10 days of postnatal age.) Tracer studies utilizing ^{203}Pb indicate that the rate of Pb absorption was substantially increased in the pregnant, relative to the nonpregnant, dam. Although a similar increase in ^{45}Ca absorption was also observed during pregnancy, increases in Pb absorption were enhanced by Pb pretreatment, whereas Ca absorption was independent of Pb pretreatment. From this data it is concluded that the apparently greater sensitivity of postnatal development on prenatal Pb exposure is secondary to enhanced Pb absorption in the pregnant rat. In vitro metabolic studies in isolated cerebral cortex slices taken from 15-day-old rat pups exposed to Pb revealed increased glucose and oxygen consumption in response to elevations in the potassium concentration of the incubation media. This evidence of metabolic uncoupling in the immature rat cerebral cortex may be causally related to the measured delays in brain development.

Effects of Zinc Deficiency on Lead Toxicity in Rats

P.J. Bushnell and E.D. Levin. NEUROBEHAV TOXICOL TERATOL 1983 May-Jun;5(3):283-8.

Authors' abstract: The effect of zinc deficiency on the toxicity of dietary lead in rats — as measured by body weight changes, tissue lead retention, and choice behavior in a complex maze — was studied. Weanling rats were fed a zinc-free semipurified diet supplemented via drinking solutions with either 2 or 20 ppm zinc and 0, 10, or 100 ppm lead. During exposure, choice behavior was quantified in a radial maze. After a 3-week period on diet, the animals' physical development was assessed, and the retention of lead and zinc in bone and brain were determined by atomic absorption spectroscopy. Zinc deficiency slowed rats' weight gain, did not affect relative organ weights, increased the retention of lead in both calvarium and in brain, and reduced the accuracy of performance in the maze. Lead exposure at 100 ppm reduced body weight and increased relative organ weights and reduced maze accuracy at both 10 and 100 ppm. Neither treatment affected the rats' running speed through the maze. Lead exposure and zinc deficiency exerted additive effects on body weight. The two treatments did not interact in the behavioral assay.

Postabsorptive Effect of Increased Dietary Zinc on Toxicity and Removal of Tissue Lead in Rats

F.L. Cerklewski. J NUTR 1984 Mar;114(3):550-4.

Author's abstract: Weanling male albino rats were fed a diet containing 12 ppm zinc and 200 ppm lead for 3 weeks. At the end of this time a representative number of samples were collected to determine tissue zinc and lead, inhibition of the lead-sensitive liver enzyme δ-amino-

levulinic acid dehydratase (ALAD), and urinary δ-aminolevulinic acid (ALA). Dietary lead exposure was terminated, and the remaining rats were fed diets containing either 12 or 200 ppm zinc. Analyses were repeated at 5-day intervals over a 15-day period after lead exposure. As expected, inhibition of liver ALAD, excretion of urinary ALA, and soft tissue lead content rapidly decreased after lead was removed from the diet, approaching control levels by day 15. Although high dietary zinc increased the zinc content of plasma, liver, and tibia, there was little or no therapeutic effect on recovery of liver ALAD, urinary ALA excretion, or on the removal of lead from liver, kidney, or tibia. Removal of red blood cell lead, however, was greater for rats fed the high zinc diet. Results of this study indicate that the postabsorptive interaction between zinc and lead is considerably less important than the previously reported intestinal interaction.

The In Vitro Effects of Zinc and Manganese on δ-Aminolevulinic Acid Dehydratase Activity Inhibited by Lead or Tin

M. Chiba and M. Kikuchi. TOXICOL APPL PHARMACOL 1984 May;73(3):388-94.

Authors' abstract: The effects of the administration of lead and tin on δ-aminolevulinic acid dehydratase (5-aminolevulinate hydro-lyase, ALAD, EC 4.2.1.24) activity in human, rabbit, and mouse blood were studied in vivo. In addition the ability of zinc, manganese, and dithiothreitol (DTT) to restore ALAD activity in the blood of lead- or tin-treated subjects was examined in vitro. Manganese, zinc, and DTT restored ALAD activity in vitro. The optimal concentration of zinc required in vitro was 10^{-4} M in blood of lead-exposed humans and lead- or tin-administered mice, and 10^{-3} M in blood of rabbits treated with either lead or tin. Even at the optimal concentration of zinc, the reactivating effect was incomplete, the highest recovery being about one-third of the control activity. However, the simultaneous addition of zinc and DTT increased ALAD activity to levels comparable with those of controls. Manganese was less effective than zinc in restoring ALAD activity in vitro; the effective dose was 10^{-2} M in the blood of lead-exposed subjects, but little effect was noted in tin-treated subjects. Manganese was as effective as DTT in protecting against the inhibition of ALAD activity in vitro by excessive zinc. In contrast, DTT restored ALAD activity completely in the blood of tin-treated rabbits and produced about an 80% recovery of enzyme activity in the blood of tin-treated mice, but only a 35% recovery in the blood of lead-treated rabbits. These results suggest that the mechanisms by which lead and tin inhibit ALAD activity are different.

Applications of Nuclear Technologies for In Vivo Elemental Analysis

S.H. Cohn, K.J. Ellis, D. Vartsky, and L. Wielopolski. NEUROTOXICOLOGY (Park Forest Il) 1983 Fall;4(3):34-47.

Authors' abstract: The objectives of this Department of Energy-sponsored program are (1) to improve existing nuclear techniques and (2) to develop new techniques for the analysis and solution of both medical problems and those associated with environmental pollution. Measurement facilities developed, to date, include a unique whole body counter (WBC); a total body neutron activation facility (TBNAA); and a partial body activation facility (PBNAA). A variation of the prompt γ neutron activation technique for measuring total body nitrogen has been developed to study body composition of cancer patients and the effect of nutritional regimens on the composition. These new techniques provide data in numerous clinical studies not previously amenable to investigation. The development and perfection of these techniques provide unique applications of radiation and radioisotopes to the early diagnosis of certain diseases and the evaluation of therapeutic programs. The PBNAA technique has been developed and calibrated for in vivo measurement of metals. Development has gone forward on prompt γ neutron activation for the measurement of cadmium, x-ray fluorescence (XRF) for measurement of lead, and nuclear resonance scattering (NRS) for measurement of iron. Other techniques are being investigated for in vivo measurement of metals such as silicon and beryllium. Cardinal to all toxicological studies of Cd and other metal pollutants is an accurate and sensitive noninvasive technique for measuring organ burdens. In keeping with the mission of Brookhaven, we have made these facilities available to qualified scientists and members of the medical community throughout the world.

Liver Hyperplasia and Regression After Lead Nitrate Administration

A. Columbano, G.M. Ledda-Columbano, P.P. Coni, M. Vargiu, G. Faa, and P. Pani. TOXICOL PATHOL 1984;12(1):89-95.

Authors' abstract: The effect of a single intravenous injection of lead nitrate on liver was investigated in male Wistar rats. Lead nitrate at 5 and 10 μmoles/100 g of body weight stimulated a nineteenfold increase in the incorporation of ^{3}H-thymidine into liver DNA and resulted in temporal changes in DNA synthesis, as determined by assays of specific activity. Thirty-six hours after lead nitrate administration, the incorporation of ^{3}H-thymidine reached its maximum and returned to normal levels within 3 days. A significant increase in the number of cells entering mitosis at 36 hours indicated the capacity of lead to stimulate liver cell proliferation. Enlarge-

ment of the liver after lead treatment was also observed in both female Wistar rats as well in male Fischer rats. This stimulatory effect of lead on liver growth was reversible; during the involution of the liver, cell death morphologically similar to the one described as apoptosis was observed in histological sections of liver from animals sacrificed 4-7 days after lead treatment.

Influence of Heavy Metals on Synaptic Transmission: A Review

G.P. Cooper and R.S. Manalis. NEUROTOXICOLOGY (Park Forest Il) 1983 Winter;4(4):69-83.

Authors' abstract: The acute effects of Pb^{++}, Cd^{++}, and Hg^{++} have been studied on the amphibian neuromuscular junction. These heavy metal ions primarily affect those presynaptic mechanisms that underlie neurotransmitter release; no significant postsynaptic effects were observed. All experiments were performed on the isolated sciatic nerve/sartorius muscle preparation. Conventional electrophysiological techniques using intracellular recordings were used to monitor acetylcholine (ACh) release. Ringer solutions usually contained high Mg^{++} and low Ca^{++} concentrations so that endplate potentials (EPP's) could be recorded under contraction-free conditions. Pb^{++}, Cd^{++}, and Hg^{++} were added to the Ringer solutions as chloride salts. Of the two forms of transmitter release, Pb^{++} blocked one (evoked release or EPP amplitude) and stimulated the other (the rate of spontaneous release or miniature endplate potentials [MEPP] frequency). When a preparation was first exposed to a moderate dose of Pb^{++}, the EPP amplitude decreased within about 1-2 min; however, at that time, the MEPP frequency was just beginning to increase. Low concentrations of Pb^{++} often reduced the EPP greatly without altering the MEPP frequency. Evidence is provided for a competitive interaction between Pb^{++} and Ca^{++} ions in evoked release, which is believed to occur on the extracellular side of the nerve terminal. The dissociation constant between Pb^{++} and the presynaptic Ca^{++} receptor is about 1 μM. The increase in MEPP frequency is assumed to be due to an intracellular action of Pb^{++}, which may reduce the ability of nerve terminal organelles to sequester Ca^{++} and thereby increase the intracellular concentration of ionized Ca^{++}. Cd^{++} also blocks evoked ACh release by a competitive inhibitory mechanism similar to that for Pb^{++}. Cd^{++} is slightly less potent than Pb^{++}, the dissociation constant for Cd^{++} being around 2.8 μM. In contrast to Pb^{++}, Cd^{++} does not increase resting MEPP frequency. Hg^{++} is unique in that it first causes an increase in evoked ACh release and then a sudden and complete blockade; the MEPP frequency follows a similar time course. The mechanism underlying these effects of Hg^{++} is uncertain.

Heavy Metals: Effects on Synaptic Transmission

G.P. Cooper, J.B. Suszkiw, and R.S. Manalis. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):247-66.

Authors' abstract: The acute effects of Pb^{++}, Cd^{++}, and Hg^{++} on synaptic transmission were studied on the in vitro sciatic nerve-sartorius muscle preparation of the frog by using electrophysiological techniques. Biochemical procedures were used to examine the effects of Pb^{++} and Cd^{++} on in vitro preparations of synaptosomes. In the electrophysiological studies Pb^{++} was shown to be a powerful competitive inhibitor of action potential-evoked release of acetylcholine (ACh), as judged by its depressant effects on the amplitude of endplate potentials (EPPs). The dissociation constant between Pb^{++} and the presynaptic Ca^{++} receptor is about 1 μM. Pb^{++} also increases spontaneous transmitter release as determined by the frequency of miniature endplate potentials (MEPPs). The increase in MEPP frequency is assumed to be due to an intracellular action of Pb^{++} to reduce the ability of nerve terminal organelles to buffer Ca^{++} and, thereby, increases the intracellular concentration of Ca^{++}. Cd^{++} also blocks evoked ACh release by a competitive inhibitory mechanism that appears similar to that for Pb^{++}. The dissociation constant for Cd^{++} is about 2.8 μM. In contrast to Pb^{++}, Cd^{++} does not increase resting MEPP frequency. Hg^{++} is unique in that it first causes an increase in evoked ACh release and then a sudden and complete blockade; the MEPP frequency follows a similar time course. The mechanism underlying these effects of Hg^{++} is uncertain. In rat brain synaptosomes, Pb^{++} and Cd^{++} competitively inhibit the K^{+}-stimulated influx of $^{45}Ca^{++}$. The dissociation constants for the interaction of Pb^{++} and Cd^{++} with Ca^{++} channels are 1.1 μM and 2.2 μM, respectively. These data strongly support the idea that the electrophysiological effects of Pb^{++} and Cd^{++} on the EPP are due to a reduction of voltage-gated Ca^{++} entry into presynaptic nerve terminals.

Placental Transfer and Fetal Distribution of Lead in Mice After Treatment with Dithiocarbamates

B.R. Danielsson, A. Oskarsson, and L. Dencker. ARCH TOXICOL 1984 Mar;55(1):27-33.

Authors' abstract: The distribution of intravenously administered lead (^{203}Pb-acetate; 50 nmol/kg b.w.) was studied by means of autoradiography and impulse counting in pregnant C57BL mice (day 18) treated orally with dithiocarbamates. Diethyldithiocarbamate (DEDTC), disulfiram or thiram (2 X 1 mmol/kg b.w.), or vehicle (gelatine) alone, was given by gavage 2 h before and immediately after the injection of lead. All three dithiocarbamates, especially thiram, changed the dis-

tribution pattern of lead. Thiram and DEDTC had the greatest effect at 4 h after lead administration, disulfiram at 24 h. In the mother, most notably the brain concentration increased (seventyfold for thiram at 4 h), but that of erythrocytes and skeleton decreased (fiftyfold and fourfold, respectively). The total fetal concentration unexpectedly showed only a moderate increase (approximately twofold for thiram), which may be due partly to the low maternal plasma lead concentration. The partition within the fetal tissues was, however, changed by the dithiocarbamates in much the same way as in the mothers, e.g., the fetal brain of thiram-treated animals had increased by a factor 15, whereas skeletal and blood concentrations were lowered compared with controls. In melanin-containing structures of the maternal and fetal eyes a dramatic increase in lead concentration resulted from dithiocarbamate treatment (lead ions are known to bind to melanin in vitro). The pattern of changes in lead distribution caused by dithiocarbamates is consistent with the formation in the body of lipid-soluble lead-dithiocarbamate complexes that pass biological barriers more easily than inorganic lead (to brain, fetus, melanocytes, etc.), probably followed by a dissociation of the complexes in the tissues.

The Effects of Lead Administration During Development on Lithium-Induced Polydipsia and Dopaminergic Function

D.L. DeHaven, M.R. Krigman, J.J. Gaynor, and R.B. Mailman. BRAIN RES 1984 Apr 16;297(2):297-304.

Authors' abstract: Previous studies have demonstrated that postnatal (days 2-29 of life) administration of lead (200 mg/kg/day by gavage) to Long-Evans rats caused permanent increases in lithium-induced polydipsia (LIP). These lead-induced increases in LIP were apparently not of renal origin, did not occur in animals treated with lead after day 30, and persisted for at least 6 months. The present studies have narrowed the dose-time window for lead-induced increases in LIP. The first study showed that continuous administration of lead (200 mg/kg/day, p.o.) in the form of lead acetate during days 2 to 9 of life caused increases in LIP ($P = 0.022$). Although lead-induced increases in LIP were not statistically significant ($P = 0.084$) for the group administered lead from days 9 to 19, the lack of a significant difference between the 2- to 9- and 9- to 19-day groups suggested that lead treatment during either of these time periods would result in LIP increases. Lead administration between days 19 and 29 of life was not effective in increasing LIP ($P = 0.8$). In the second study, a single dose of lead (200 mg/kg/day) was administered either on day 5 or 15 of life. Concentrations of lead in the blood on day 30 of life averaged 23.2 μg/10 ml for treated rats versus 4.8 μg/100 ml for controls. When tested at approximately 90 days of age, both groups showed significant increases in LIP ($P = 0.028$). The rats from this second study were also examined for changes in nigrostriatal dopamine function, since this pathway is known to be essential for LIP.

Creatine Kinase-BB Isoenzyme in Rat Plasma After Chronic Lead Intoxication

T. Delahunty. BIOCHEM BIOPHYS RES COMMUN 1984 Nov 30;125(1):192-8.

Author's abstract: Creatine kinase (CK) activity in plasma obtained noninvasively from healthy, adult Sprague-Dawley male rats was found to be 528 ± 270 U/L ($N = 17$), a value which was 7 times that obtained in human specimens. Agarose gel electrophoresis revealed that the only detectable CK isoenzyme present was CK-BB, in contrast to the human serum isoenzyme,which was CK-MM. Furthermore, it was found that the rat CK-BB could be detected by using a radioimmunoassay (RIA) technique designed to quantitate human CK-BB occasionally present in blood after brain injury (rat CK-BB = 84.5 ± 55.2 μg/L, $N = 17$; human CK-BB: not detectable). It was thus possible to calculate the CK-BB specific activity (SA) in rat plasma by using total CK assay and RIA (rat CK-BB SA = 6.25 ± 3.87 U/μg, $N = 17$). When six rats (156 ± 23 g) were treated with lead acetate in the drinking water (26 mM) for 3 weeks, the CK-BB SA rose to 18 ± 5.8 U/μg ($P < .02$). At this point, the electrophoresis pattern of the CK-BB showed a transient change from a single band to a doublet. The dose was then increased to 52 mM for 6 weeks, during which time the CK-BB SA declined steadily to 1.6 ± 0.6, a level significantly less than that of the untreated animals ($p < .02$). The results suggest that chronic lead treatment evokes a biphasic response in CK-BB SA with the initial release of enzyme of high SA from tissues. Further treatment apparently results in an inactivation of the enzyme within lead-sensitive tissues.

Hepatic Cholesterol in Lead Nitrate Induced Liver Hyperplasia

S. Dessi, B. Batetta, E. Laconi, C. Ennas, and P. Pani. CHEM BIOL INTERACT 1984 Mar;48(3):271-9.

Authors' abstract: Wistar rats treated with lead nitrate were used in these experiments to provide evidence of the possible correlation between hyperplasia, induced cholesterol synthesis, and the levels of glucose-6-phosphate dehydrogenase (G-6-PD) in the liver. Lead treatment increases liver weight, hepatic cholesterol esters, and the relative content of free cholesterol. An increase of the incorporation of tritiated water in free and cholesterol esters was also observed. The effect of lead resulted in an increase of hepatic G-6-PD at all times considered. The correlation between these parameters and hyperplasia is discussed.

Effects of $Na_2CaEDTA$ on Lead Deposits in Rabbit Osseous Tissue

J. Doniec, B. Trojanowska, M. Trzcinka-Ochocka, and I. Garlicka. TOXICOL LETT 1983 Oct-Nov;19(1-2):1-5.

Authors' abstract: Radiochemical and autoradiographic methods were used for ^{210}Pb determination after $Na_2CaEDTA$ administration to rabbits. ^{210}Pb was determined in soft tissues, compact and trabecular bones, and growing microareas on the endosteum of the long bone. After $Na_2CaEDTA$ injection, lead was depleted from 'new' deposits mainly on the growing surface of both trabecular and compact bones.

Biological Availability of Lead in a Paint Aerosol. 2. Absorption, Distribution and Excretion of Intratracheally Instilled Lead Paint Particles in the Rat

D.L. Eaton, D. Kalman, D. Garvey, M. Morgan, and G.S. Omenn. TOXICOL LETT 1984 Sep;22(3):307-13.

Authors' abstract: Four groups of rats received by intratracheal instillation (1) a lead chromate paint particulate suspension, (2) lead tetraoxide suspension, (3) lead acetate solution, or (4) saline. Lead-dosed animals received an equivalent dose of 1 mg lead/kg body weight. Distribution of lead was monitored through assays of urine, feces, and tissues (lung, bone, muscle kidney, liver) obtained post-mortem 5 weeks after exposure. δ-Aminolevulinic acid dehydratase (ALA-D) activity was measured to determine the effect of lead on heme biosynthesis. The vast majority of the dosed lead in the paint matrix remained in the lung. In contrast, in the lead acetate-dosed animals, little remained in the lung, but significant elevations were found in bone and kidney. Blood ALA-D was significantly depressed in the lead acetate-treated animals, but was not significantly different from control animals in the animals dosed with lead paint or lead tetraoxide. These findings suggest that lead chromate in an alkyd resin paint matrix is poorly absorbed from the lung compared with lead acetate and lead tetraoxide.

Gastrointestinal Absorption of Lead in Chicks: Involvement of the Cholecalciferol Endocrine System

S. Edelstein, C.S. Fullmer, and R.H. Wasserman. J NUTR 1984 Apr;114(4):692-700.

Authors' abstract: The role of dietary calcium and phosphorus in modifying the intestinal absorption of lead and also the effect of lead ingestion on the metabolism of cholecalciferol were studied in chicks. The efficiency of absorption of ^{203}Pb and ^{47}Ca was increased when the animals were fed a low calcium diet and treated with cholecalciferol. The synthesis of the vitamin D-induced calcium-binding protein (CaBP) was correspondingly increased. When the chicks were depleted of vitamin D and repleted with 1,25-dihydroxycholecalciferol [$1,25(OH)_2D_3$] as their only source of the vitamin, the absorption of both ^{47}Ca and ^{203}Pb was unaffected by dietary calcium levels, and no change in CaBP levels occurred. Low dietary intake of phosphorus resulted in an increase in ^{47}Ca and ^{203}Pb absorption and in CaBP synthesis when the animals were treated with cholecalciferol. However, when the birds were repleted with $1,25(OH)_2D_3$, the intestinal absorption of ^{47}Ca and of ^{203}Pb was increased, as well as the intestinal CaBP levels. Intracardial injection of increasing doses of $1,25(OH)_2D_3$ to rachitic chicks resulted in a concomitant increase in ^{203}Pb absorption in a manner that correlated with the degree of synthesis of CaBP. Ingestion of lead by the chicks was found to impair growth and renal production of $1,25(OH)_2D_3$, resulting in lowered circulating and intestinal content of the hydroxylated metabolites of cholecalciferol.

Tissue Mineral Levels in Victims of Sudden Infant Death Syndrome. II. Essential Minerals: Copper, Zinc, Calcium, and Magnesium

M.M. Erickson, A. Poklis, G.E. Gantner, A.W. Dickinson, and L.S. Hillman. PEDIATR RES 1983 Oct;17(10):784-7.

Authors' abstract: Deficiencies of various vitamins and minerals per se have been suggested as possible causes of sudden infant death syndrome (SIDS). Further, a deficiency of essential minerals may lead to enhanced toxicity of toxic elements, in particular lead and cadmium. To explore the possibility of mineral deficiencies or interactions with the toxic metals, lead and cadmium, we obtained lung, liver, kidney, and rib specimens at autopsy from 66 SIDS infants and 23 infants who died suddenly from other causes. Tissue copper, zinc, calcium, and magnesium were measured by atomic absorption spectroscopy. No differences were found between SIDS and non-SIDS for any element in any tissue except for more magnesium in the liver ($P < 0.0001$) and less copper in the lungs ($P < 0.02$) in the SIDS group. Only sporadic interactions between toxic and essential elements could be found. We found no evidence of any essential mineral deficiencies per se or significant interactions of essential and toxic minerals that might potentiate the effects of toxic metals. The physiologic significance, if any, of the higher liver magnesium and lower lung copper found in SIDS is unclear.

Tissue Mineral Levels in Victims of Sudden Infant Death Syndrome. I. Toxic Metals — Lead and Cadmium

M.M. Erickson, A. Poklis, G.E. Gantner, A.W. Dickinson, and L.S. Hillman. PEDIATR RES 1983 Oct;17(10):779-84.

Authors' abstract: Lung, liver, kidney, and rib specimens were obtained at autopsy from 66 sudden infant death syndrome (SIDS) infants and 23 infants who died suddenly from other causes between the ages of 4-26 wk. Tissue levels of lead and cadmium were measured by atomic absorption spectroscopy and are expressed as micrograms/gram dry weight. Because these metals are cumulative with age in storage tissues, the levels were corrected for age (adjusted to age 13 wk). The SIDS liver and rib specimens contained significantly more lead than non-SIDS tissues (liver, 1.095 μg/g versus 0.761 μg/g, $P < 0.05$; rib, 1.754 μg/g versus 1.041 μg/g, $P < 0.01$, respectively). There were no significant differences in cadmium concentration between the SIDS and non-SIDS tissues. All four tissues showed significant increases with age in both lead and cadmium concentrations in SIDS. The increase in lung lead concentration with age was significantly greater in SIDS than in non-SIDS cases, $P < 0.05$. In non-SIDS only kidney cadmium showed an increase with age ($P < 0.0001$). These data collectively suggest an increased exposure of the SIDS infant to lead either prenatally and/or postnatally. Any physiologic effects of the increased tissue lead levels are unknown. They may be only a marker of the known epidemiology of SIDS.

The Immunotoxicity of Selected Environmental Chemicals, Pesticides and Heavy Metals

J.H. Exon. PROG CLIN BIOL RES 1984;161:355-68.

Author's abstract: It is an established fact that certain environmental chemicals, pesticides, and heavy metals can alter the immune response of laboratory animals and probably humans as well. In some instances, the immune system appears to be exquisitely sensitive to these agents compared with other toxicologic parameters. Both stimulation and suppression of immune responses have been demonstrated in contaminant-exposed animals. Although most data accumulated to date pertain to effects in small laboratory rodents, there is little reason to believe that similar quantifiable effects do not occur in domestic and food-producing animals because of basic functional similarities of the immune system of mammals in general.

Comparison of the In Vivo and In Vitro Effects of Lead on the pH-Activity Relationship of Human Erythrocytic δ-Aminolaevulinic Acid Dehydratase

J.P. Farant and D.C. Wigfield. BR J IND MED 1984 Aug;41(3):406-11.

Authors' abstract: The effect of lead in vitro on the pH-activity relationship of human erythrocytic δ-aminolevulinic acid dehydratase (δ-ALAD) and on the assessment of lead exposure with ratios of δ-ALAD activity measured at specific pH values was investigated. The addition of lead nitrate to whole blood at concentrations ranging from 0.40 to 8.1 μmol Pb^{2+}/l, for periods of contact ranging from 16 h to 20 days at 4° C, resulted in a time- and dose-dependent shift of the enzyme's pH optimum to a more acid value. The pH optimum shift obtained at raised lead concentrations or after long periods of contact at 4° C, in both, closely approximated that observed in vivo. The loss of enzyme activity, however, was significantly less in vitro than that in vivo for similar whole blood lead concentrations. These findings indicate that the presence of trace amounts of lead in blood collection devices can seriously affect results obtained with the pH activity ratio method of assessing lead exposure.

Organic Lead and Histological Parameters of Brain Development

N.J. Ferris and B.G. Cragg. ACTA NEUROPATHOL (Berl) 1984;63(4):306-12.

Authors' abstract: Relatively little work has been done on the structural effects of organic lead in the central nervous system (CNS), although this form of lead may be a significant fraction of total brain lead. We tested a number of easily measured light-histological parameters of neuronal development in rats for sensitivity to (a) normal growth between 18 and 28 days of life and (b) the effect of weekly injections of tetramethyl lead (TML), administered from 1 week after conception until postnatal day 6. Several of the histological parameters were found to be sensitive to normal growth, but none showed any effect of organic lead treatment. This was so, despite a small but significant decrease in brain weight, and a significant increase in body/brain weight ratio, with tetramethyl lead treatment. The body/brain weight ratio was the parameter most sensitive to tetramethyl lead treatment. Possible reasons for the disparity between weight and histological parameters are discussed, with reference to previous workers' findings concerning the effects of organic lead on the development of myelin in the CNS and the availability of organic lead to brain tissue.

Role of Selenium in Protection Against Lead Intoxication

S.J. Flora, S. Singh, and S.K. Tandon. ACTA PHARMACOL TOXICOL (Copenh) 1983 Jul;53(1):28-32.

Authors' abstract: The administration of selenium concomitantly with lead in rats restrained the lead-induced enzymuria, proteinuria, enhanced urinary excretion of δ-aminolevulinic acid, inhibition of the activities of certain renal enzymes, blood δ-aminolevulinic acid dehydratase, and blood, liver, and kidney uptake of lead. The protective effect of selenium against lead toxicity may be attributed to a competition between selenium and lead for binding with the functional bioligands or to the in vivo formation of lead selenide.

Investigation of the Effect of Metal Ions on the Reactivity of Thiol Groups in Human 5-Aminolaevulinate Dehydratase

P.N. Gibbs, M.G. Gore, and P.M. Jordan. BIOCHEM J 1985 Feb 1;225(3):573-80.

Authors' abstract: The reaction of human 5-aminolevulinate dehydratase with 5,5'-dithiobis-(2-nitrobenzoic acid) (Nbs_2) results in the release of 4 molar equivalents of 5-mercapto-2-nitrobenzoic acid (Nbs) per subunit. Two of the thiol groups reacted very rapidly (groups I and II), and their rate constants were determined by stopped-flow spectrophotometry; the other two thiol groups (groups III and IV) were observed by conventional spectroscopy. Titration of the enzyme with a 1 molar equivalent concentration of Nbs_2 resulted in the release of 2 molar equivalents of Nbs and the concomitant formation of an intramolecular disulphide bond between groups I and II. Removal of zinc from the holoenzyme increased the reactivity of groups I and II without significantly affecting the rate of reaction of the other groups. The reactions of the thiol groups in both the holoenzyme and apoenzyme were little affected by the presence of Pb^{2+} ions at concentrations that strongly inhibit the enzyme, suggesting that Zn^{2+} and Pb^{2+} ions may have independent binding sites. Protein fluorescence studies with Pb^{2+} and Zn^{2+} have shown that the binding of both metal ions results in perturbation of the protein fluorescence.

Regulation of Lead Inhibition of δ-Aminolevulinic Acid Dehydratase by a Low Molecular Weight, High Affinity Renal Lead-Binding Protein

P.L. Goering and B.A. Fowler. J PHARMACOL EXP THER 1984 Oct;231(1):66-71.

From authors' abstract: The bioavailability of Pb in kidney is mediated in part by binding to high affinity cytosolic Pb-binding proteins (PbBP) of 11,500 (11.5K) and 63,000 (63K) daltons, which are not found in liver. Renal δ-aminolevulinic acid dehydratase (ALAD) is also markedly more resistant to Pb inhibition than hepatic ALAD in vivo. This study was undertaken to evaluate further the differences in sensitivity of renal and hepatic ALAD to Pb and to determine if inhibition of hepatic ALAD by Pb could be reversed by addition of partially purified PbBP from kidney to liver cytosol. Rat liver or kidney cytosol was incubated with Pb over a concentration range of 0.1 to 10 μM. Renal ALAD was 7.5 times more resistant to Pb inhibition than that in liver. Kidney cytosol and ^{203}Pb were incubated before Sephadex G-75 or G-150 column chromatography to isolate the 11.5K and 63K PbBP, respectively. Inhibition of hepatic ALAD activity by Pb was partially reversed by a single addition of semipurified 11.5K PbBP in the presence of 0.1 to 0.4 μM Pb, but no protective effect was observed at higher concentrations of Pb. This effect was not observed with the 63K PbBP added at an equivalent high affinity binding capacity or with bovine serum albumin added at an eightfold higher total protein concentration. Reversal of Pb-induced inhibition of hepatic ALAD activity was dependent on the concentration of 11.5K PbBP in the reaction mixture. Kinetic analysis of either hepatic or renal ALAD activity at an IC_{50} concentration of Pb indicated a noncompetitive inhibition pattern.

Effect of Heavy Metals on Human Rheumatoid Synovial Cell Proliferation and Collagen Synthesis

R.L. Goldberg, S.R. Kaplan, and G.C. Fuller. BIOCHEM PHARMACOL 1983 Sep 15;32(18):2763-6.

Authors' abstract: The dose-dependent effects of heavy metals on cell proliferation, collagen synthesis, and noncollagen protein synthesis were studied in early passage cultures of human synovial cells exposed to 1-100 μM concentration of gold, silver, mercury, cadmium, or lead for 5 days. The incorporation of [^{3}H] thymidine into trichloroacetic acid insoluble material was inhibited 50% by each of the heavy metals at concentrations between 1 and 10 μM. Gold, lead, and mercury (10 μM) decreased the DNA content of the cultures by $< 15\%$; silver (10 μM) and cadmium (10 μM) resulted in decreased DNA content, which was attributed to cytotoxicity. A dose-dependent inhibition of [^{3}H]proline incorporation into bacterial collagenase-resistant (noncollagen) protein was observed after incubation with 10 μM mercury, lead, and silver. During incubations with 10 μM gold and cadmium, collagenase-resistant protein accumulation increased. All the heavy metals except for gold inhibited collagen accumulation to a greater extent than noncollagen protein accumulation. Gold (10 μM) stimulated the amount of collagen produced per cell, and the percentage of col-

lagen to total protein was increased 50%. The rate of collagen accumulation in medium decreased during incubation with 10 μM silver, mercury, cadmium, and lead. The stimulation of collagen synthesis may be a unique property of gold related to the therapeutic indices of gold, compared with other heavy metals, in rheumatoid arthritis.

Brain Capillaries: A Target for Inorganic Lead Poisoning

G.W. Goldstein. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):167-75.

Author's abstract: Like nutrients and waste products, toxic metals enter and leave the brain by passing through the endothelial cells of brain capillaries. In contrast to most systemic organs, the endothelial cells of the brain microvasculature are sealed together by tight junctions. The result is a blood-brain barrier produced by a continuous layer of endothelial cells. Since heavy metals most likely pass through these cells to enter the brain, it is not surprising that the metals may accumulate within and injure the capillary cells. This review will consider some of the features that distinguish endothelial cells in the brain from those in systemic organs. Special consideration will be given to processes that may influence the transport and toxicity of inorganic lead.

Intracellular Sites of Toxic Metals

R.A. Goyer. NEUROTOXICOLOGY (Park Forest Il) 1983 Fall;4(3):147-56.

Author's abstract: In summary, this brief overview of the cellular localization of toxic metals in renal tubular cells demonstrates a spectrum of mechanisms for the sequestration of the metals. Common features are affinity for a metal-binding protein, such as insoluble acidic nuclear proteins or the soluble, low-molecular-weight metallothionein. Accumulation in lysosomes follows assimilation of metal containing protein by lysosomes or autophagocytosis of degenerating metal containing mitochondria. Currently available methods have not demonstrated the presence of metals in immune complex deposits in glomerular basement membrane and epithelial cells. The principal methods employed for the localization of metals within cells have been X-ray microanalysis of thin preparation of tissue, or direct analysis of subcellular fractions by atomic absorption spectroscopy or detection of radioactive metal.

Plasma Membrane Protection Against the Acute Effects of Inorganic Lead on the Respiratory Rates of Intact Liver Cells

J.J. Guttas, G.T. Carter, and B.A. Horwitz. J TOXICOL ENVIRON HEALTH 1983 Oct-Dec;12(4-6):731-6.

Authors' abstract: To evaluate the acute effects of inorganic lead on oxidative metabolism in hepatocytes, we isolated intact liver cells from hamsters and incubated with solutions of $PbCl_2$. These cells were found to be relatively resistant to respiratory inhibition as compared with liver homogenates. That is, in the presence of 1 mM $PbCl_2$, the rate of oxygen consumption of the intact cells was approximately 6% less than that of controls. In contrast, the respiratory rates of liver homogenates treated with 1 mM $PbCl_2$ were about 70% lower than controls. The resistance of the intact cells persisted even after 4 1/2 h of incubation with the lead and appears to reflect the protective influence of the plasma membrane.

Influence of Triethyl Lead on the Activity of Enzymes of the Ascites Tumor Cell Plasma Membrane and Its Microviscosity

E.W. Haeffner, H.P. Zimmermann, and C.J. Hoffmann. TOXICOL LETT 1984 Nov;23(2):183-8.

Authors' abstract: The influence of triethyl lead (TriEL) on the activity of plasma membrane-bound enzymes of Ehrlich ascites tumor cells and on membrane fluidity has been investigated. TriEL completely inhibits the $(Na^+ - K^+)$-ATPase in its membrane-bound and even more pronounced in its solubilized form between 5 and about 20 μM. It also alters the microviscosity of the isolated plasma membrane up to a temperature of about 30° C, but it does not have any influence on the fluidity of the membrane-derived liposomes. From these data it is concluded that the inhibitor may interact directly with the catalytic subunit of the $(Na^+ + K^+)$-ATPase and may not exert its influence by interfering with the membrane lipids.

Neuropathological Lesions in Experimental Lead Toxicosis of Dogs

A.N. Hamir, N.D. Sullivan, and P.D. Handson. J COMP PATHOL 1984 Apr;94(2):215-31.

Authors' abstract: Light microscopical examinations were carried out on the central and peripheral nervous systems of nine dogs maintained on a high-fat-low-calcium diet and dosed orally with a mixture of lead chloride, lead bromide, and lead sulphate. Microscopic lesions were present in seven (78%) of the lead-treated dogs. Cerebrocortical lesions comprising spongiosis, vascular hypertrophy, and gliosis predominated. These lesions were bilateral, had a predilection for gyri, and were located mainly in the parietal and frontal cortex. There were bilaterally symmetrical spongiform changes in the brain stem. The cerebellum had spongiform changes in the roof nuclei, and in the lingula there was spongiosis of the Purkinje cell layer and vacuolation of Purkinje cells. Axonal degeneration was evident in a sciatic nerve of one dog. In a second experiment, designed to study the early ultrastructural changes in the

brains of dogs with lead intoxication, two groups of dogs, one on a commercial balanced diet and the other fed a high-fat-low-calcium diet, were given similar amounts of lead. Cytoplasmic accumulation of lipid was found in the cerebrovascular pericytes of all dogs treated with lead, but vascular changes were otherwise not obvious. Quantitative evaluation of numbers of blood vessels by light microscopy revealed an apparent increase in all dogs receiving lead. This increase in vascularity was greatest in the dogs fed the high-fat-low-calcium diet.

Toxicological Considerations in the Assessment of Lead Exposure

P.B. Hammond, R.L. Bornschein, and H. Zenick. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):53-66.

Authors' abstract: Many uncertainties remain today concerning effects of lead on the nervous system, particularly in regard to levels of lead exposure causing minimal brain dysfunction in children. Past studies in children have failed to define adequately the nature of the effect, the critical period and duration of exposure, and the role of other factors in rendering the developing organism susceptible to lead. Prospective studies now underway should contribute greatly to the resolution of these issues. The studies propose to monitor both lead exposure and behavior at fixed intervals from birth for up to 5 years. The index of exposure in all studies is blood lead concentration. Test batteries vary considerably among studies, but most propose to include the Bayley Scales and the McCarthy Scales. These design features should greatly facilitate comparison of results across the studies. In the design of animal studies certain standardized features across studies also seem desirable, particularly concerning the characterization of lead exposure. Repeat measures of blood lead concentration in rats receiving lead via dams' milk and via water after weaning indicate that the response of individual animals is extremely variable, both as to the pattern of lead build-up and as to the degree of exposure. It is to be expected that biological responses would vary accordingly. It also follows that dose-response and dose-effect relationships in animal studies should be analyzed taking into account this problem. Data analysis should consider the dose and response of each animal individually. In the design of dosage regimens, the profiles of blood lead levels in adults and young children reported in the literature are useful guidelines in the design of exposure regimens. Many studies are concerned with nonbehavioral aspects of lead toxicity, e.g., disposition of neurotransmitters, morphological features of brain maturation, and alterations in blood-brain barrier function. It would be extremely useful to relate the findings to some fairly standardized behavioral end point as well as to well-defined blood lead profiles.

Free Erythrocyte Protoporphyrin (FEP) and Zinc Protoporphyrin (ZnP) as Biological Parameters for Lead Poisoning

K. Harada and H. Miura. INT ARCH OCCUP ENVIRON HEALTH 1984;53(4):365-77.

Authors' abstract: Lamola et al. (1974) reported that free erythrocyte protoporphyrin (FEP) is not present as free type protoporphyrin (FPP) but rather is chelated with zinc in lead poisoning and iron deficiency anemia. In our fluorometric study of FEP and zinc protoporphyrin (ZnP) in erythrocytes of lead-poisoned rabbits and lead workers, the coexistence of ZnP and FPP was observed in the severe stage of acute lead poisoning in rabbits. The ratio of ZnP to FEP in erythrocytes decreased with the progress of lead intoxication, and the amount of FPP was greater than that of ZnP in the severe stage of intoxication. This FPP accumulated in the erythrocytes was easily converted to ZnP by incubation of the hemolysate with zinc. On the other hand, increased protoporphyrin (PP) in bone marrow was present as FPP in lead intoxication. From these results, ZnP in peripheral erythrocytes is considered to be a secondary product, not a primary one. Therefore, determining total FEP (FPP + ZnP) by the acid solvent extraction method might be more reasonable than using ZnP determination as the biological parameter of lead poisoning. We propose that erythrocyte porphyrin in lead intoxication should be expressed as FEP, not as ZnP, for the parameter. The present study also suggests that the form of erythrocyte FPP in erythropoietic protoporphyria (EPP) patients is a little different from that in lead-poisoning patients because of its high chelation reactivity with zinc.

Relationship Between Hematopoietic Parameters and Behavioral Measures in Lead-Exposed Rats

L. Hastings, H. Zenick, P. Succop, T.J. Sun, and R. Sekeres. TOXICOL APPL PHARMACOL 1984 May;73(3):416-22.

Authors' abstract: The effects of low-level lead (Pb) exposure on learning tasks in developing rats were investigated, and the results were correlated with individual hematopoietic indices. Pups received exposure via the dams' milk; dams were exposed to either 0-, 545-, or 1,090-ppm Pb during the lactation period. At day 30 of age, half of the high Pb group was placed on distilled water; the remaining groups continued on the same exposure regimens as their dams. On days 20, 30, and 90, blood samples for all rats were obtained via cardiac puncture. Each sample was analyzed for Pb concentration, free erythrocyte protoporphyrin (FEP), hematocrit, and hemoglobin. Beginning at day 90, all rats were tested on a battery of tasks designed to investigate the following questions: (1) to what degree lead exposure interferes

with reversal learning; (2) whether changing of task requirements adversely affects acquisition of a new task; (3) to what extent task difficulty contributes to lead-induced deficits; and (4) whether lead exposure affects the capacity to retain information over short or long periods of time. The actual testing paradigms included spatial discrimination with reversal, visual discrimination with reversal, and visual discrimination task with delay. No significant differences were observed among any of the groups on any of the tasks. Correlation of individual learning scores with individual measures of hematopoietic function also failed to reach significance. These findings indicate that at low exposure levels, lead has little appreciable effect on learning and memory function as measured by these tasks.

Lead Toxicity in the Pregnant Rat. I. The Effect of High-Level Lead on δ-Aminolevulinic Acid Dehydratase Activity in Maternal and Fetal Blood or Tissues

M. Hayashi. ENVIRON RES 1983 Feb;30(1):152-60.

Author's abstract: A study was made of the effects of administration of 500 ppm of lead in the drinking water of pregnant rats and their fetuses. The δ-aminolevulinic acid dehydratase (ALAD) activity of erythrocytes in lead-treated dams showed 82.7% and 74.8% inhibition on days 18 and 21 of pregnancy, respectively. ALAD activity of erythrocytes in the lead-treated fetuses showed 59.7% and 73.0% inhibition on days 18 and 21 of pregnancy, respectively. ALAD activities in the liver and placenta were not significantly different between the lead-treated and control animals. The lead concentrations of blood and liver in the lead-treated dams and fetuses were higher than in the control animals, but the lead level of amniotic fluid was not significantly different from that of the control animals. Significant correlations were observed between maternal and fetal blood lead, liver lead, and erythrocyte ALAD, but there was no significant correlation between maternal and fetal liver ALAD.

Uptake of Pb by Human Skeleton and Comparative Metabolism of Pb and Alkaline Earth Elements

M.J. Heard and A.C. Chamberlain. HEALTH PHYS 1984 Dec;47(6):857-65.

Authors' abstract: Measurements of the retention of ^{47}Ca and of ^{203}Pb were made following their administration by intravenous injection. Translocation to bone was measured by γ counting the feet of subjects. Uptake by bone of ^{203}Pb was comparatively slow, and extrapolation to the whole skeleton indicated that 20% of the dose had been taken up within 20 days. By that time, a similar fraction of the dose had been excreted in urine. These results are consistent with Kehoe's (Ke61) long-term balance studies on two human subjects given stable Pb orally. Uptake by bone of ^{47}Ca was about 1.5-2 times the amount excreted in urine. Both the uptake by bone and its excretion in urine were more rapid than that of ^{203}Pb because of the greater attachment of the latter to red blood cells. However, the plasma clearance rate for Pb, like that of Sr, was greater than that of Ca.

Uptake of Lead by Humans and Effect of Minerals and Food

M.J. Heard, A.C. Chamberlain, and J.C. Sherlock. SCI TOTAL ENVIRON 1983 Sep;30:245-53.

Authors' abstract: In several series of experiments, volunteers have ingested ^{203}Pb as chloride (a) in distilled water, with or without stable Pb carriers, while fasting, (b) with varying amounts of added minerals Ca and P, (c) with hot or alcoholic beverages between normal meals, and (d) in the course of meals. Furthermore, volunteers have eaten lamb's liver and kidney into which ^{203}Pb had been incorporated by injection into the animal before slaughter, and spinach that had taken up ^{203}Pb from its roots. Fasting subjects absorbed 40%-50% of the ^{203}Pb, taken in distilled water, irrespective of the addition of Pb carrier up to 100 μg per dose. When taken with tea or coffee, uptake averaged 14%, and with beer 19%. Much lower uptakes, ranging from 3% to 7%, were found when ^{203}Pb was taken in volunteers with a meal, or incorporated in offal or vegetables that were eaten as part of a meal, or when taken with large amounts of calcium or phosphate.

Maturation of Resistance to Lead Encephalopathy: Cellular and Subcellular Mechanisms

D. Holtzman, C. DeVries, H. Nguyen, J. Olson, and K. Bensch. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):97-124.

Authors' abstract: The rat pup fed inorganic lead has been studied extensively as an animal model of human lead encephalopathy. As in man, the sensitivity of the brain to lead toxicity is age-dependent. Pups given daily lead feedings for 1 week beginning in the first week of life show pathologic changes (i.e., hemorrhage, edema, and neuronal necrosis) throughout the brain, including the cerebral cortex and cerebellum. Pups begun on daily lead feedings for 2 weeks between 10-18 days of age show similar pathologic changes almost entirely confined to the cerebellum. Pups receiving very large quantities of lead for 2 weeks beginning at 20 or 24 days of age develop only minimal edema or no changes by light microscopy. We have proposed that the effects of lead on cellular aerobic energy metabolism are important in the pathogenesis of the encephalopathy in the developing

brain. Early in the course of lead feedings begun at 14 days of age, isolated cerebellar mitochondria show a loss of respiratory control. During the second week of lead feedings, respiration with NAD-linked substrates is inhibited in cerebellar mitochondria, but not in cerebral mitochondria, from these animals. Cerebral mitochondrial respiration in pups fed lead from birth also is inhibited, whereas both cerebral and cerebellar mitochondrial respiration in lead-fed adults is not affected. Isolated brain mitochondria exposed to lead in vitro show similar changes: an initial respiratory stimulation (probably reflecting an energy-coupled uptake of lead) and a secondary inhibition of dehydrogenases located in the mitochondrial matrix. Lead also may compete with calcium for brain mitochondrial carrier or binding sites. During maturation, the brain appears to become resistant to lead toxicity by sequestering lead away from the mitochondrial site of action. This hypothesis is based upon the observations that: (1) the in vitro effects of lead are the same in immature and mature cerebellar mitochondria; (2) the cerebral and cerebellar lead concentrations are the same in immature encephalopathic and mature encephalopathy-resistant lead-fed animals; and (3) cerebellar mitochondria from animals fed lead from 14 days of age contain much more lead than cerebral mitochondria from these animals and cerebellar mitochondria from lead-fed adults. This hypothesis is supported further by the results of recent electron microscopic and elemental microprobe studies of lead distribution in the brains of animals fed lead beginning at 14-18 days of age.

The Role of Wildlife Species in the Assessment of Biological Impact from Chronic Exposure to Persistent Chemicals

M. Hutton. ECOTOXICOL ENVIRON SAFETY 1982 Oct;6(5):471-8.

Author's abstract: Investigators assessing chemical toxicity have regularly placed reliance upon experimental studies in which environmentally unrealistic exposure regimens are used. This approach ignores the long-term low-level nature of environmental exposure, which facilitates the development of factors that modify the toxicity of such chemicals. Examples of such adaptive mechanisms are taken from the author's own studies. Factors discussed include the development of protective trace element interactions in target organs, the induction of specific metal-binding proteins, and the alteration of the distribution of chemicals at the organ and organelle levels. Exposure-response investigations in wildlife are not restricted to the organism level, and the impact of an environmentally released chemical upon breeding success and population dynamics can also be investigated. Disadvantages and problems associated with this kind of study, such as multiple pollutant exposure and variability in response, are considered.

Increase of δ-Aminolevulinic Acid Dehydratase (ALAD) in Rat Erythrocytes in Lead Poisoning

M. Kajimoto, M. Kondo, M. Niwa, T. Suzuki, H. Kimura, A. Sasaki, and G. Urata. ARCH TOXICOL 1983 Jan;52(1):1-11.

Authors' abstract: The well-known fact that the activity of δ-aminolevulinic acid dehydratase (ALAD: EC 4.2.1.24) is reduced in red cells of animals with lead poisoning was found to be upset, by using a modified method of Gibson's original procedure, for determination of activated ALAD activity. The modified method involves adding 0.2 mM Zn^{2+} and then preheating the enzyme solution at 60° C for 5 min before following Gibson's original procedure. With this methodological modification, the ALAD activity of erythrocytes of rats poisoned with lead was found to be increased. Furthermore, the enzyme was purified from the peripheral blood of lead-poisoned rats. ALAD protein in peripheral blood was also determined by single radial immunodiffusion by using rabbit anti-serum raised against rat liver ALAD. As the result, the ALAD activity obtained from the modified method was found to be directly proportional to the absolute amount of enzyme proteins determined both chemically and immunochemically. The modified method for measuring true ALAD content in blood cells in lead poisoning is more reliable than previous ones.

Biological Availability of Lead in a Paint Aerosol. 1. Physical and Chemical Characterization of a Lead Paint Aerosol

D. Kalman, R. Schumacher, D. Covert, and D.L. Eaton. TOXICOL LETT 1984 Sep;22(3):301-6.

Authors' abstract: This study was conducted to determine the physical and chemical characteristics of an aerosol of lead-based paint, generated in an industrial spray operation, that might influence the biological availability of lead present in inhaled aerosols. Paint aerosols were collected, and mass-size distribution was determined by using a portable cascade impactor under actual occupational conditions. About 2% of the particulate mass collected was in the respirable range (< 10 μm mean aerodynamic diameter), although the maximum airborne concentration of lead was found to be 2-3 mg/m^3. The lead concentration in a dried aerosol was very resistant to chemical digestion. Analysis by X-ray diffraction, atomic absorption spectroscopy, and inductively coupled plasma emission spectroscopy showed about 11% lead by dry weight, although the wet weight concentration of lead reported by the manufacturer was 12.8%.

Triethyllead and Cerebral Development: An Overview

G. Konat. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):87-96.

Author's abstract: The immature brain is unduly vulnerable to the toxic effects of triethyllead (Et_3Pb). Both brain growth and main developmental events in the tissue are appreciably restrained by this neurotoxin. Generally, the susceptibility of brain cells to Et_3Pb appears to diminish with age. The major cellular alterations in the affected tissue include the destruction of cell processes and swelling and vacuolization in the pericaryon. The effect of Et_3Pb-induced poisoning is one of hypomyelination as seen from the prominent reduction in the content of cerebral myelin. Myelin-producing cells (oligodendrocytes) seem to be particularly vulnerable to Et_3Pb relative to other components of the tissue. Furthermore, the toxin specifically hampers the process of myelin membrane assembly. The inhibitory effects of Et_3Pb can be attributed to the interaction of this amphiphilic compound with cellular membranes and with the process of their biogenesis.

Inhibition of the Pentose Phosphate Shunt by Lead: A Potential Mechanism for Hemolysis in Lead Poisoning

N.A. Lachant, A. Tomoda, and K.R. Tanaka. BLOOD 1984 Mar;63(3):518-24.

Authors' abstract: Recent investigations have disclosed a decrease in pentose phosphate shunt activity in hereditary pyrimidine 5'-nucleotidase deficiency. Clinical lead poisoning is associated with an acquired decrease in pyrimidine 5'-nucleotidase activity. The current investigations were undertaken (1) to determine if pentose shunt activity was decreased in erythrocytes exposed to lead and (2) to compare the mechanism of inhibition to that seen in hereditary pyrimidine 5'-nucleotidase deficiency. Normal erythrocytes incubated with lead acetate in vitro demonstrated increased Heinz body formation, decreased reduced glutathione, a positive ascorbate cyanide test, and a reversible suppression of pentose shunt activity in the intact erythrocyte. Lead acetate added to normal red cell hemolysates markedly inhibited the activities of glucose-6-phosphate dehydrogenase (G6PD) and phosphofructokinase. The mean K_is of lead for glucose-6-phosphate and nicotinamide adenine dinucleotide phosphate (NADP) for G6PD were 1.5 μM and 2.1 μM, respectively, which is within the range of intraerythrocytic lead concentrations found in clinical lead poisoning. Magnesium enhanced the ability of lead to inhibit G6PD. Thus, the shortened erythrocyte survival in lead poisoning appears to be due, in part, to increased oxidant sensitivity secondary to inhibition of G6PD and the pentose shunt. The mechanism of shunt inhibition is, in part, similar to that seen in hereditary pyrimidine 5'-nucleotidase deficiency.

Lead and Liver Cell Proliferation. Effect of Repeated Administrations

G.M. Ledda-Columbano, A. Columbano, and P. Pani. AM J PATHOL 1983 Dec;113(3):315-20.

Authors' abstract: The effect of repeated treatments with lead on hepatic cell proliferation was investigated in male Wistar rats. The animals were given intravenous injections of lead nitrate once every 10 days for 30 and 80 days. At the end of the experimental regimen, enlargement of the liver, accompanied by an increase in hepatic DNA content, was observed. A significant enhancement in the incorporation of labeled thymidine into hepatic DNA was found in lead-treated rats at the time intervals mentioned above, when compared with controls. An increase in the number of liver cells involved in mitosis was also observed in lead-treated animals. Analysis of serum glutamic-pyruvic transaminase and histologic observations did not show any sign of cell death at the time points examined. These results indicate that liver cells exposed to repeated treatments with lead undergo proliferation. However, a progressive reduction in the capacity of hepatic cells to divide was found in rats given repeated administrations of the metal, when compared with the extent of cell proliferation induced by a single dose of lead nitrate.

The Toxic Effects of Heavy Metals on Rat Bone Marrow In Vitro Erythropoiesis: Protective Role of Hemin and Zinc

J.D. Lutton, N.G. Ibraham, M. Friedland, and R.D. Levere. ENVIRON RES 1984 Oct;35(1):97-103.

Authors' abstract: The effects of gold (Au), lead (Pb), and cadmium (Cd) on rat bone marrow in vitro erythropoiesis (CFUE) were studied. Au was found to be significantly toxic to CFUE growth at concentrations as low as 10^{-9} M, whereas Pb and Cd displayed toxicity at 10^{-7} M. Addition of Pb plus Cd in combination had a greater toxic effect on CFUE growth than when the metals were added singly, and the toxic effect of Cd was reduced when zinc (Zn) was added in combination to the cultures. When hemin (10^{-6} M) was added to cultures containing 10^{-6} M Au, Pb, or Cd, CFUE numbers were obtained that were equivalent to control cultures without hemin. Thus, hemin exerted a protective effect on erythropoiesis in the presence of otherwise toxic amounts of Au, Pb, and Cd. It is concluded that Au, Pb, and Cd have toxic effects on in vitro erythropoiesis and that this toxicity may be overcome in part by Zn or hemin. The possible involvement of the heme biosynthetic and degradative pathways is discussed with respect to these results.

Concurrent Exposure of Lead and Manganese to Iron-Deficient Rats: Effect on Lipid Peroxidation and Contents of Some Metals in the Brain

K.M. Malhotra, R.C. Murthy, R.S. Srivastava, and S.V. Chandra. J APPL TOXICOL 1984 Feb;4(1):22-5.

Authors' abstract: Iron-deficient rats were coexposed to manganese and lead to study lipid peroxide formation and contents of lead, manganese, copper, iron, zinc, and calcium in the brain. Concurrent exposure to lead and manganese increased the lipid peroxidation potential of the brain in iron-deficient rats. The concentration of lead, manganese, and copper in the brain of iron-deficient rats increased to a greater magnitude after concurrent exposure to manganese and lead, compared with that observed after the exposure of either of the metals alone. Since copper is a potent inhibitor of transport ATPase in the brain, its significant increase, coupled with increased lipid peroxidation in the brain of iron-deficient rats, may be responsible for enhanced susceptibility of iron-deficient rats to the neurotoxic effects after the combined exposure to lead and manganese.

Metal Binding by Pharmaceuticals. Part 5. Interaction of Cd(II), Ni(II) and Pb(II) with the Intracellular Hydrolysis Products of the Anti-Tumour Agent ICRF 159 and Its Inactive Homologue ICRF 192

P.M. May, M.J. Willes, D.R. Williams, and A.M. Creighton. AGENTS ACTIONS 1984 Oct;15(3-4):448-53.

Authors' abstract: Formation constants for the cadmium(II), nickel(II), and lead(II) complexes of DL-NN'-dicarboxamidomethyl-NN'-dicarboxymethyl-1,2-diaminopropane (ICRF 198) and the 1,2-diaminobutane homologue (ICRF 226) have been measured potentiometrically at 37° C and I = 150 mmol dm-3 [NaCl]. In all titrations a competing ligand, known to complex strongly with the metal ion, and having its formation constants predetermined, was employed. The constants are used in computer simulation models to assess the relative efficacy of the agents in mobilizing these metals from plasma proteins into low-molecular-weight complexes, and the results are compared with those for known chelating agents. It is shown that the lead mobilizing potential of the agents is greater than either EDTA or D-penicillamine; they are, however, less adept in the removal of cadmium and nickel than other established agents.

Neonatal Lead Exposure in Rats: II. Effects on the Hippocampal Afterdischarge

M. McCarren and C.U. Eccles. NEUROBEHAV TOXICOL TERATOL 1983 Sep-Oct;5(5):533-40.

Authors' abstract: Male Sprague-Dawley rats were exposed to lead from parturition to weaning via the dams' milk. Dams were provided with drinking water containing 1.0 (LL), 2.5 (ML), or 5.0 (HL) mg/ml lead acetate or 1.25 (C) mg/ml sodium acetate. Beginning at 15 weeks of age, characteristics of the electrically elicited hippocampal afterdischarge (AD) and its alteration by phenytoin (PHT) were assessed in these rats. A separate group of rats was sacrificed at 20 weeks for hippocampal metal analysis. Increases in primary AD duration were observed in LL and ML and were significant in ML. Significantly fewer wet dog shakes occurred in all lead groups. HL animals displayed shorter rebound AD's. All groups responded to PHT with increases in primary AD duration, but the increases in the ML and HL groups were significantly greater than in the C group. Hippocampal lead, zinc, and copper concentrations were not different from those found in controls. It is concluded that a brief lead exposure can have persistent effects on hippocampal function and that these effects are not due to altered hippocampal metal concentrations. The findings are discussed in relation to the known effects of postnatal lead exposure on hippocampal neuronal development.

Neonatal Lead Exposure in Rats: I. Effects on Activity and Brain Metals

M. McCarren and C.U. Eccles. NEUROBEHAV TOXICOL TERATOL 1983 Sep-Oct;5(5):527-31.

Authors' abstract: Upon parturition, Sprague-Dawley dams were administered 1.0 (LL), 2.5 (ML), or 5.0 (HL) mg/ml of lead acetate or 1.25 mg/ml sodium acetate (C) in their drinking water. Pups were weaned to tap water at 22 days of age. The developmental pattern of neonatal activity was characterized by monitoring spontaneous activity of single pups for 30 minutes on days 12, 14, 16, 18, 20, and 22, and for 1 hour in adults. Brains were removed at weaning for subsequent analyses of lead, zinc, and copper. The effects of lead on neonatal activity were considered to be minor because only the ML group differed significantly from C and exhibited hyperactivity on day 16. Adult activity levels, however, were decreased in a dose-dependent fashion. At 22 days of age, whole brain metal analyses revealed a dose-dependent increase in lead levels and a decrease in zinc. These results do not strongly support a hypothesis of lead-induced neonatal hyperactivity.

Spectral Analysis of Kindled Hippocampal Afterdischarges in Lead-Treated Rats

M. McCarren, G.A. Young, and C.U. Eccles. EPILEPSIA 1984 Feb;25(1):53-60.

Authors' abstract: Male rats were exposed to lead from parturition through weaning. When subjected to electrical hippocampal kindling as adults, although there were no alterations in the kindling rates, lead-treated animals

were found to differ from controls in several other respects. In contrast to controls, lead-treated animals did not show an increase in afterdischarge (AD) duration with kindling, and the power spectrum of the AD did not shift to a higher peak frequency. There was a clear dose-related effect of lead on the spectra of the kindled AD, which in lead-treated groups was characterized by greater power in the low-frequency bands. These data indicate that long-lasting dysfunction can occur following a brief neonatal lead exposure. Power spectral techniques may be useful for future studies in neurotoxicology and epilepsy.

Subcellular Distribution of Lead in Cultured Rat Hepatocytes

R.A. Mittelstaedt and J.G. Pounds. ENVIRON RES 1984 Oct;35(1):188-96.

Authors' abstract: A clear understanding of the sequence and molecular mechanism of the events involved in lead toxicity is hampered by a lack of information about lead compartmentation within the cell. As part of a continuing effort to identify the mechanism by which lead affects cellular functions, we examined the subcellular distribution of ^{210}Pb in cultured hepatocytes. The cells were isolated, labeled, homogenized in sucrose-N-[(2-hydroxyethyl)piperazine]-N'-2-ethanesulfonic acid buffer, and fractionated into mitochondrial, microsomal, and cytosolic components by differential centrifugation. Complete fractionation of the cells revealed that 71% of the cellular ^{210}Pb was associated with the mitochondria, 5% with the microsomes, and 24% with the cytosol. A modified, rapid fractionation procedure indicated that 45% of the cellular lead was associated with both the mitochondria and the cytosol and 10% with the microsomes. When the cells were separated into total particulates and cytosol with a single centrifugation, 22% of the ^{210}Pb was associated with the soluble fraction. The process of homogenization and fractionation of the isolated hepatocytes altered the intracellular distribution of ^{210}Pb. This experimental approach to studying the localization of lead may be compromised by the redistribution of ^{210}Pb during the extensive centrifugations and resuspensions required for subcellular fractionation and suggests that the subcellular distribution patterns of ^{210}Pb obtained by the fractionation of cells reflects the distribution of lead in the homogenate rather than the distribution of ^{210}Pb in the intact cell.

Lead Distribution in the Saliva and Blood Fractions of Rats After Intraperitoneal Injections

N. Mobarak and A.Y. P'an. TOXICOLOGY 1984 Jul;32(1):67-74.

Authors' abstract: Sprague-Dawley rats were treated with 1, 2, or 3 intraperitoneal injections of lead acetate (100 mg/kg) and sacrificed 24 h, 3 days, 7 days, 14 days, and 21 days after the last injection. Lead concentration was determined by flameless atomic absorption spectroscopy (AAS) technique in whole blood, plasma, plasma filtrate, saliva, and submaxillary gland tissue. The concentration of lead in saliva was about 5% of whole blood lead concentration and around 61% of plasma filtrate lead level. Saliva lead concentration was significantly related both to whole blood lead concentration and plasma filtrate lead concentration ($r = 0.78$, $P < 0.001$; $r = 0.80$, $P = 0.001$, respectively). Lead was present in the submaxillary gland tissue; the amount of lead increased with increasing amounts administered.

In Vitro Effects of Lead, Mercury and Cadmium on the Enzymic Activity of Red-Blood Cell Pyrimidine 5'-Nucleotidase

B. Mohammed-Brahim, J.P. Buchet, A. Bernard, and R. Lauwerys. TOXICOL LETT 1984 Feb;20(2):195-9.

Authors' abstract: The decrease of pyrimidine 5'-nucleotidase (P5N) in human erythrocytes, detected in persons occupationally exposed to lead (Pb), is not an in vitro artefact resulting from the release of lead during erythrocyte hemolysis but is a true reflection of the enzyme activity in vivo. Like Pb, mercury (Hg) and cadmium (Cd) ions exhibit an important in vitro inhibitory action on the P5N enzymic activity. However, when the metals are preincubated as metallothionein complexes with P5N preparations, their inhibitory power disappears.

Kidney Urokinase Activity Following Acute Exposure to Lead

D.M. Nicholls and M.J. Kuliszewski. BIOCHEM PHARMACOL 1984 Jan 15;33(2):181-6.

Authors' abstract: Urokinase activity was measured in kidney homogenate fractions obtained 2 days after injecting rats with 0.5 mg Pb^{2+}/100 g body weight. The activity was higher in the membrane-containing fractions than in the soluble supernatant fractions and was markedly higher in the preparations derived from the lead-treated rats. The kidney poly(A)$^+$ RNA was obtained from these animals and translated in a rabbit reticulocyte lysate system. In the preparations obtained from the lead-treated rats, there was an increased synthesis of a protein, believed to be urokinase, of pI 8.6 and molecular weight (M_r) 45,000.

Some Toxic Effects of Lead, Other Metals and Antibacterial Agents on the Nervous System — Animal Experiment Models

L. Olson, H. Bjorklund, A. Henschen, M. Palmer, and B. Hoffer. ACTA NEUROL SCAND [Suppl] 1984;100:77-87.

Authors' abstract: Modern man is chronically exposed to lead levels in the biosphere, several times higher than the natural level that once existed. There is much concern about the possible adverse effects of this population-wide low-level lead exposure, particularly on the developing organism, where the central nervous system may be a primary target for lead. We have developed animal test systems that permit temporal and spatial discrimination of possible effects of lead and other potentially neurotoxic agents in the environment on the developing central nervous system, as well as on different types of peripheral nerves in the adult individual. In one experimental design, defined areas of the fetal rat brain are grafted to the anterior chamber of the eye of adult rat recipients that are exposed to lead (1% PbAc in drinking water). Such grafts will become vascularized from the host iris and continue their development in oculo. Thus, the grafted brain tissue and the host brain will share circulation and therefore be exposed to exactly the same amounts of lead simultaneously. Studies of cerebellar grafts revealed that although there was a normal gross cytological development in the presence of lead, there was a severe, permanent impairment of the spontaneous discharge rates of the grafted Purkinje neurons as observed with electrophysiological techniques long after cessation of the lead treatment. The host Purkinje neurons were not affected. A similar, although less dramatic, impairment of cerebellar function could then be demonstrated in intact animals when newborn rats were given lead (8 mg PbAc/kg i.p.) during the first 20 days of life and then studied as adults. In other areas of the fetal central nervous system grafted to the eye, lead caused disturbed growth (substantia nigra, cortex cerebri). A screening technique for potentially harmful effects on autonomic and sensory nerve terminals in adult rats makes use of intraocular injections of agents to be tested. Morphological and histochemical changes of the innervation apparatus of the iris are then studied in iris whole-mount preparations. Lead causes an adrenergic hyperinnervation of the iris. Computer-based image analysis revealed severe degenerative effects by hexachlorophene and chlorhexidine. These studies demonstrate the usefulness of the intraocular grafts and the intraocular injection technique and the need to apply both structural and functional techniques in order to detect possible neurotoxic actions of xenobiotics. The techniques have revealed hitherto unknown toxic actions of lead on cerebellar function.

Chronic Lead Exposure of the Developing Brain: Electrophysiological Abnormalities of Cerebellar Purkinje Neurons

M.R. Palmer, H. Bjorklund, D.A. Taylor, A. Seiger, L. Olson, and B.J. Hoffer. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):149-66.

Authors' abstract: This manuscript reviews our recent research concerning electrophysiological effects of chronic low-level lead exposure on the developing brain. We found that although growth, survival, and histological organization of in oculo cerebellar grafts appear normal after perinatal exposure to blood lead levels of 450 to 550 μg/liter, the physiological activity of Purkinje neurons in these lead-treated grafts is abnormally low after discontinuation of lead treatment. On the other hand, chronic low-level lead exposure postnatally via systemic injections or perinatally via the drinking water did not alter in situ cerebellar Purkinje cell activity. Moderate systemic doses (2 mg/kg) did cause a persistent slowing of Purkinje neuron firing rates; however, this effect was much smaller than in intraocular cerebellar grafts. The slowing may be mediated by lead actions on various transmitter systems. We have found that chronic lead induces catecholaminergic neurons to hyperinnervate target areas. Perhaps this hyperinnervation is initiated by the postsynaptic lead-induced blockade of the electrophysiological effects of norepinephrine, which we have previously observed in the cerebellum in situ and in cerebellar grafts in oculo.

Some Effects of Lead at Mammalian Neuromuscular Junction

J.B. Pickett and J.C. Bornstein. AM J PHYSIOL 1984 Mar;246(3 Pt 1):C271-6.

Authors' abstract: The effect of lead on transmitter release was investigated in a rat phrenic nerve-hemidiaphragm preparation by using conventional microelectrode techniques. Lead reduced the number of quanta released by a nerve stimulus (m) in a dose-dependent fashion. As extracellular Ca^{2+} concentration ($[Ca^{2+}]_o$) was varied in the absence of lead, a linear relationship between ln(m) and ln($[Ca^{2+}]_o$) was obtained. Lead shifted the relationship between ln(m) and ln($[Ca^{2+}]_o$) to the right without altering the slope. This suggested that lead competed with Ca^{2+}, which was confirmed by using a modified Lineweaver-Burk plot. Lead inhibits Ca^{2+} entry into frog sympathetic preganglionic nerve terminals, and a similar mechanism may underlie this present finding; such a mechanism, however, could not explain all the observed actions of lead. Lead increased the frequency of spontaneous quantal release in a dose-dependent manner, and 10^{-4} M lead doubled the magnitude of facilitation of evoked release seen with five stimuli at 60 Hz. It is suggested that these effects result

from inhibition of some, or all, of the nerve terminal's Ca^{2+} sequestration mechanisms.

Protoporphyrin Hepatopathy. Effects of Cholic Acid Ingestion in Murine Griseofulvin-Induced Protoporphyria

M.B. Poh-Fitzpatrick, J.A. Sklar, C. Goldsman, and J.H. Lefkowitch. J CLIN INVEST 1983 Oct;72(4):1449-58.

Authors' abstract: Short-term effects of cholic acid ingestion on hepatic accumulation, fecal excretion, and blood levels of protoporphyrin were studied in vivo in griseofulvin-induced protoporphyric mice. Experimental mice that received feed with 2% griseofulvin and 0.5% cholic acid were compared with control mice that received feed with 2% griseofulvin for 4 wk. Five mice from each group were assessed each week for liver and blood porphyrin levels. Fecal protoporphyrin was compared weekly in the total pooled output of each population. Mean protoporphyrin levels were significantly lower for liver ($P < 0.0001$), erythrocytes ($P < 0.05$), and plasma ($P < 0.05$), and higher for feces ($P < 0.001$) for the mice that were fed cholic acid. Microscopic protoporphyrin deposits, inflammation, necrosis, and dysplasia were more severe in livers of control mice. A second experimental design compared four regimens in the feed given to all mice after a 1-wk induction with 2% griseofulvin: (a) 0.5% cholic acid, (b) no adulterant, (c) 2% griseofulvin and 0.5% cholic acid, and (d) 2% griseofulvin. No difference in protoporphyrin removal from livers of mice in groups 1 and 2 was observed after 1 and 2 wk of these regimens. The apparent reduction in hepatic protoporphyrin content in mice of group 3 as compared with group 4 at weeks 2 and 3 was not significant at $P < 0.05$. These data suggest that, in selected circumstances, hepatic protoporphyrin secretion may be enhanced in protoporphyric disease states by bile salt supplementation.

Effect of Lead Intoxication on Calcium Homeostasis and Calcium-Mediated Cell Function: A Review

J.G. Pounds. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):295-331.

Author's abstract: The interaction between lead and essential metals is a complex, well recognized, but poorly understood phenomenon. Dietary deficiencies or excesses of certain essential metals may alter the absorption, elimination, or dose response of lead. Lead, in turn, may alter the homeostasis and function of essential metals. This review will be limited to the effect of lead on calcium, an essential metal with elaborate systemic and cellular homeostatic mechanisms and innumerable second messenger and coupling-factor functions. Lead may ultimately perturb calcium-regulated or calcium-mediated functions (a) directly by interfering with calcium transport or storage processes, e.g., Ca^{2+} transport proteins, calcium gates, etc.; (b) indirectly by altering cell functions required for calcium homeostasis, e.g., energy production, plasma membrane permeability, etc.; (c) by substitution of Pb^{2+} for Ca^{2+} at functionally important calcium binding sites, e.g., calmodulin. Although any individual study may not provide adequate experimental verification of the causal role of perturbations of calcium metabolism and function as the primary toxic lesion of lead-intoxication, the collective observations of many studies do strongly support lead-calcium interactions as an important functional lesion in lead-intoxicated organelles, cells, tissues, and organ systems.

Effects of Lead on the Renal Response to Extracellular Volume Expansion

W.J. Powers, Jr. and E.C. Foulkes. PROC SOC EXP BIOL MED 1985 Mar;178(3):367-72.

Authors' abstract: Subacute lead exposure has been observed to inhibit the natriuretic response to isotonic saline expansion in adult female rats. Three-week exposure to 0.5% lead acetate in drinking water resulted in a moderately high blood lead concentration of 57 μg/100 ml and up to 60% inhibition of the natriuretic response to extracellular volume expansion. This ability of lead to inhibit natriuresis following volume expansion (an induced stress) may be a more sensitive index of lead poisoning than alterations of renal function in non-stressed animals. Lead exposure had no effect on glomerular filtration rate (GFR) or plasma aldosterone concentrations, and in the presence of large doses of DOCA (a mineralocorticoid) this inhibitory effect of lead was still persistent. Amiloride completely blocked the antinatriuretic effect of lead in volume-expanded lead-poisoned animals, causing a twofold increase in water and electrolyte excretion while having minimal effects on volume-expanded controls. It is concluded that lead interferes with the action of a "third factor" controlling natriuresis.

In Vitro Study on Lead and Alcohol Interaction and the Inhibition of Erythrocyte δ-Aminolevulinic Acid Dehydratase in Man

D. Prpic-Majic, S. Telisman, and S. Kezic. SCAND J WORK ENVIRON HEALTH 1984 Aug;10(4):235-8.

Authors' abstract: The effect of lead (Pb) and ethanol (EtOH) interaction on the inhibition of erythrocyte δ-aminolevulinic acid dehydratase (ALAD) was investigated in human blood in vitro. Two different doses of ethanol (equivalent to 16.28 mmol of EtOH/l of blood

and 108.53 mmol of EtOH/l of blood) and lead (equivalent to 2.17 μmol of Pb/l of blood and 4.34 μmol of Pb/l of blood) were examined separately and in combination. The dose-effect (EtOH-ALAD) relationship for a wide range of ethanol concentrations (0-217.06 mmol of EtOH/l of blood) was also investigated. The results obtained indicate that ethanol by itself does not inhibit ALAD, whereas lead does it readily. Neither ethanol concentration significantly altered ALAD activity. The dose-effect (EtOH-ALAD) relationship did not reveal any inhibitory effect of ethanol on ALAD either; however, a weak trend towards increased ALAD activity was found. The effect of ethanol combined with lead indicated no significant difference as compared with the effect of the same dose of lead per se; however, a weak trend towards decreased ALAD activity was found. These findings support the hypothesis that the effect of ethanol on the transient inhibition of ALAD activity in vivo does not occur directly, but possibly through the intermediary action of lead from the body lead pool.

Effects of Lead Exposure on Peripheral Nerve in the Cynomolgus Monkey

D.A. Purser, K.R. Berrill, and S.K. Majeed. BR J IND MED 1983 Nov;40(4):402-12.

Authors' abstract: We examined the relationship between blood lead concentration and nerve conduction velocity using the cynomolgus monkey as a model for human lead poisoning, with lead dose and blood lead concentration maintained under controlled conditions, to determine whether nerve conduction velocity could be used as an objective measure of the effects of lead on the nervous system at subclinical concentrations. Five cynomolgus monkeys were maintained at a blood lead concentration of 90-100 μg Pb/100 ml for 9 months by daily oral dosing with lead acetate (12-15 mg Pb/kg body weight). Motor nerve conduction velocity in the ulnar nerve was measured, together with blood lead concentrations. Blood lead concentrations were proportional to lead intake, reaching a stable level within 1 to 2 weeks. Lead did not accumulate in the blood, and blood lead concentrations were found to decrease to a maintained plateau from initial high concentrations during the first 7 days of dosing. The animals showed no clinical or behavioral evidence of lead poisoning at any time during the study, although there was a progressive decrease in blood-packed cell volume, hemoglobin concentration, and erythrocyte concentration. The maximal motor nerve conduction velocity of the ulnar nerve remained constant throughout the study, although changes were observed in the conduction velocity of slowly conducting nerve fibers. At termination, intranuclear inclusions were found in the renal tubular cells of all animals, and focal areas of myelin degeneration were found in the ulnar and sciatic nerves.

Prevention of Neonatal Hyperbilirubinaemia in Nonhuman Primates by Zn-Protoporphyrin

M.K. Qato and M.D. Maines. BIOCHEM J 1985 Feb 15;226(1):51-7.

Authors' abstract: Nonhuman primates were used as a model of human neonatal hyperbilirubinemia and its chemotherapeutic suppression. High levels of heme oxygenase activity were detected in the liver and the spleen of neonatal rhesus (*Macaca mulatta*) and cynomolgus (*Macaca irus*) monkeys. When 1-day-old neonatal animals were given a single injection of Zn-protoporphyrin (40 μmol/kg, subcutaneously), serum bilirubin levels declined to nearly normal adult levels within 24 h and remained suppressed throughout the postnatal period (12 days). This treatment inhibited the activities of heme oxygenase and biliverdin reductase in the liver and the spleen, without affecting that of the brain. Zn-protoporphyrin treatment did not alter the activity of brain biliverdin reductase or increase brain bilirubin levels. The biological disposition of Zn-protoporphyrin was examined by measuring the biliary and urinary excretion of the metalloporphyrin complex, as well as its uptake and deposition in blood cells and tissues. Biliary excretion of the metalloporphyrin was minimal (0.12% over a 28-h period), and no evidence was detected for the urinary excretion of Zn-protoporphyrin. However, the concentration of metalloporphyrin in erythrocytes increased over the duration of the experiment (11 days) to such an extent that 46% of the administered compound was taken up by the cells. It appeared that the molecular basis for the sustained suppression of heme oxygenase activity and bilirubin production by Zn-protoporphyrin involved the release of the metalloporphyrin in the normal process of the degradation of fetal erythrocytes. The scope of the biological activity of Zn-protoporphyrin to alter heme-dependent processes appeared limited in nature, insofar as the microsomal contents of cytochrome P-450 and b_5, as well as the aniline hydroxylase, were similar to those of the control animals. Also, the concentration of glutathione in the liver was unchanged. These findings suggest the potential usefulness of Zn-protoporphyrin in experimental and perhaps clinical conditions in which hyperbilirubinemia occurs.

Effect of Lead Acetate on Rats Fed Diets Containing Low Levels of Folic Acid

J.I. Rader, E.M. Celesk, J.T. Peeler, and K.R. Mahaffey. DRUG NUTR INTERACT 1982; 1(2): 131-42.

Authors' abstract: Nutritional factors such as deficiencies of calcium, iron, and protein alter susceptibility to the toxic effects of lead. Although the suggestion has been made that vitamins may also influence lead toxicity, possible interactions have not been well documented.

The present studies were performed to determine if a dietary deficiency of folic acid enhances the susceptibility to rats of the toxic effects of lead acetate. Lead exposure during the development of folate deficiency resulted in alterations in two of the parameters diagnostic of the individual conditions. Decreases in erythrocyte mean corpuscular volume (MCV) occur during lead poisoning, whereas increases occur during the development of folate deficiency. In the present study, significant reductions in MCV were observed in both the control + lead and in the low folate + lead groups. The increased MCV characteristic of folate deficiency was prevented by the concomitant lead exposure. Elevations in free erythrocyte protoporphyrin (FEP) levels are characteristic of lead intoxication; in contrast, FEP levels decline during folate deficiency. In the present study, FEP levels were significantly elevated only in the control + lead group. Values in the low folate + lead group were intermediate between those of the control and the control + lead groups, but did not differ significantly from those in the low folate group. The expected lead-induced elevation in FEP levels was diminished by the reduced erythropoiesis characteristic of folate deficiency.

The Bioavailability of Iron, Lead and Cadmium via Gastrointestinal Absorption: A Review

H.A. Ragan. SCI TOTAL ENVIRON 1983 Jun;28:317-26.

Author's abstract: The primary route of entry of essential metals and most pollutant metals into the body is by gastrointestinal absorption. Although intraluminal factors influence the bioavailability of metals, the major control level of absorption probably resides in the intestinal mucosal cell. Interrelationships between various metals may affect their bioavailability at both the luminal and mucosal levels. It has also been shown that the nutritional status may have a profound influence on the absorption of some metals; iron, calcium, and protein deficiency may enhance the absorption of several pollutant metals, although this is apparently not simply an increased gut permeability to all heavy metals. Valid speculations regarding the absorption of pollutant metals is difficult since, even after several decades of intensive study, the precise mechanisms of controlling the absorption of iron and other trace metals are unknown.

Chronic Low-Lead Exposure from Birth Produces Deficits in Discrimination Reversal in Monkeys

D.C. Rice. TOXICOL APPL PHARMACOL 1985 Feb;77(2):201-10.

Author's abstract: Cynomolgus monkeys (*Macaca fascicularis*) were dosed from birth with 100, 50, or 0 μg/kg/day of lead. This protocol resulted in blood lead concentrations of 25, 15, or 3 μg/dl, respectively, before withdrawal of infant formula at 200 days of age. Blood lead concentration declined thereafter over the next 100 to 150 days to steady-state levels of 13, 11, or 3 μg/dl. At approximately 3 years of age, monkeys were tested on a series of three discrimination reversal tasks: nonspatial form discrimination, nonspatial color discrimination with irrelevant form cues, and nonspatial form discrimination with irrelevant color cues. The higher dose group was impaired relative to controls over the entire experiment (all three tasks combined), the two form discrimination tasks combined, and the form discrimination with no irrelevant cues. Deficits were most marked over the first several reversals. The lower dose group was impaired on the color discrimination task and on the last several reversals of all tasks combined. In addition, the higher dose group was impaired relative to the lower dose group over the entire experiment.

Influence of Trimethyl Lead and Inorganic Lead on the In Vitro Assembly of Microtubules from Mammalian Brain

G. Roderer and K.H. Doenges. NEUROTOXICOLOGY (Park Forest Il) 1983 Summer;4(2):171-80.

Authors' abstract: The influence of trimethyl lead (TriML) and inorganic lead (Pb) on the in vitro assembly of microtubules (MT's) from tubulin of porcine brain was studied by using turbidity measurements and electron microscopy. At concentrations of 150 to 650 μM Pb, no significant effects on the in vitro assembly of MT's could be detected by both methods. On the other hand, TriML increasingly blocked MT assembly at 100 to 200 μM and completely inhibited assembly at 300 μM TriML and higher concentrations. Application of 400 μM TriML to preassembled MT's caused an immediate drop of the optical density. Electron microscopy showed that 1 minute after addition of TriML to assembled MT's only very few intact MT's could be detected, whereas 10 minutes later MT's were completely absent. The observed increase of optical density following the TriML-induced drop was found to be due to the formation of clusters of aggregates but not to assembly of MT's. The results demonstrate that inorganic lead and trimethyl lead have different effects on the in vitro assembly of MT's. It is assumed that the selective neurotoxic effects of organic lead might be due, at least in part, to impairments of neurotubular structures and functions.

The Metabolism of Lead in Isolated Bone Cell Populations: Interactions Between Lead and Calcium

J.F. Rosen. TOXICOL APPL PHARMACOL 1983 Oct;71(1):101-12.

Author's abstract: Previous studies of lead metabolism in bone organ culture have defined, in part, an exchangeable bone lead compartment regulated by the same ions and hormones that normally control bone cell metabolism. This study was undertaken to further characterize this subcompartment of exchangeable lead and to examine possible interactions between lead and calcium in isolated bone cell populations. Bone cells, derived from mouse calvaria, were enriched for osteoclasts (OC) and osteoblasts (OB) by a sequential collagenase digestion. We found that (1) the uptake of ^{210}Pb by OC cells was rapid, and OC cells had greater avidity for lead, compared with OB cells, at concurrent time points of incubation; (2) OB cells showed very little increase in lead uptake as medium lead concentrations were increased from 6.5 to 65 μM; in contrast, the uptake of lead by OC cells was almost linear; (3) after loading OC cells with ^{210}Pb, significant release of label (approximately 15% to 30%) occurred within short time periods (≤ 2 hr) during incubations in chase medium; (4) parathyroid hormone (PTH) at physiological concentrations effected a marked increase in ^{210}Pb and ^{45}Ca uptake in OC cells; after 5 min of incubation, Pb accumulation into OC cells continued as calcium uptake markedly decreased; (5) this PTH effect on ^{210}Pb uptake was linear over PTH concentrations of 50 to 250 ng/ml; and (6) rising medium concentrations of lead (≥ 26 μM) markedly enhanced/exaggerated calcium uptake by OC cells, far above that produced by physiological concentrations of PTH. These data indicate that (1) quantitatively, OC cells are the predominant cell type in the metabolism of lead in this in vitro system of OC and OB cell monolayers; (2) mediated incorporation of lead into OC cells occurs and likely involves changes in membrane permeability effected by hormonal stimuli, such as PTH; and (3) modulations in cellular calcium metabolism induced by lead at low concentration may have the potential of disturbing multiple cell functions of different tissues that depend upon calcium as a second messenger.

Chronic Lead Administration in Neonatal Rats: Electron Microscopy of the Retina

R.M. Santos-Anderson, M.O. Tso, J.J. Valdes, and Z. Annau. J NEUROPATHOL EXP NEUROL 1984 Mar;43(2):175-87.

Authors' abstract: The morphologic effects on the retina resulting from chronic lead exposure were assessed in neonatal rats. Newborn rats nursed from dams were given a low (0.115%) or a high (4.5%) concentration of lead in their diet. At day 21 the pups were weaned to the mother's diet. The retinas of the pups were studied by electron microscopy at various ages up to day 60. High and low lead concentrations produced necrosis of photoreceptor cells and cells of the inner nuclear layer. The high lead concentration, in addition, was associated with swelling of endothelial cells of the retinal vessels and narrowing of the lumen. Increased permeability of the retinal vessels and pigment epithelium to horseradish peroxidase was also observed under the high-dose condition. The authors conclude that lead can produce direct neuronal damage and, at high doses, produces retinal vascular lesions and alteration of the blood-retinal barrier.

Absorption and Tissue Distribution of Lead in Thiamin-Replete and Thiamin-Deficient Rats

L.B. Sasser, G.G. Hall, G.R. Bratton, and J. Zmudzki. J NUTR 1984 Oct;114(10):1816-25.

Authors' abstract: Previous experimental results revealed that thiamin (vitamin B1) reduced lead (Pb) toxicity in calves and decreased tissue lead content in lead-treated calves and rodents. The objective of this experiment was to study the uptake and tissue distribution of lead in rats deprived of thiamin or given excess thiamin and to determine the effect of thiamin on lead absorption. Rats were divided into four groups and fed a thiamin-deficient or thiamin-supplemented diet. The thiamin-replete group also received daily injections of thiamin hydrochloride. Experimental diets were fed for 5 weeks, after which the rats were administered 10 μCi of ^{203}Pb acetate (25 μg lead) and killed 6, 24, 48, or 72 hours later. Lead content and concentration of tissues increased twofold in the thiamin-replete group at 24 hours after dosing, but returned to control values 24 hours later. Tissue lead concentration of the thiamin-depleted group was slightly depressed at 24 hours after dosing, but this trend was reversed at the end of the experiment. Tissue lead concentrations in the pair-fed control group were three to seven times greater than in the other treatment groups 6 hours after dosing. The results indicate that thiamin facilitated absorption and increased the amount of lead initially taken up by tissue. Thiamin may also promote more rapid release of lead from tissues.

Effects of Early Lead Exposure on Neurotransmitter Systems in the Brain. A Review with Commentary

M.K. Shellenberger. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):177-212.

Author's abstract: The mechanism by which early lead exposure alters the functional development of the brain

remains an open question. One primary avenue of approach has been to study the effects of neonatal lead exposure on neurotransmitter systems. This paper reviews the published data related to the interaction of lead with each of those systems. Further, each dosing paradigm has been evaluated with a view to experimental error and interactive variables. It was concluded that factors such as the time at which pregnant animals were shipped and mode of dosing may have been uncontrolled variables causing variability in reported results between and within laboratories. Most publications deal with the interaction of lead with catecholamine systems and with dopamine in particular. Reports of effects are highly variable, and many observations lack confirmation by other laboratories or have not been replicated. However, the bulk of observations leads to the tentative conclusion that lead does result in an altered functional state of the catecholamine systems. This is true for cholinergic function as well. Some perturbation of acetylcholine metabolism probably exists, but the specificity and significance of the effect are suspect. Reports that lead alters the functional state of GABA pathways are interesting but require confirmation. The generality and variability of effects on neurotransmitter systems questions the degree of specificity that may be expected. It is suggested that lead may effect a variable change in the functional state of all these systems by limiting glucose metabolism during periods of vulnerability.

The Effect of Lead on Photoreceptor Response Amplitude — Influence of the Light Stimulus

A.J. Sillman, D.A. Bolnick, J.B. Bosettii, L.W. Haynes, and A.E. Walter. EXP EYE RES 1984 Aug;39(2):183-94.

Authors' abstract: The mass receptor potential of the excised, superfused retina of the bullfrog was studied. Photoreceptor responses were isolated by addition of sodium aspartate to the Ringer solutions. Responses of the cones were monitored independently from responses of the rods by employing a two-flash method of stimulation that took advantage of the very different rates of rapid dark adaptation of rods and of cones. Stimulation with paired flashes of white light at regular intervals caused enhancement of rod response amplitude, in that the response grew larger with subsequent flashes until reaching a stable plateau. The degree of enhancement was directly proportional to the amount of light exposure and increased with either increasing stimulus intensity or decreasing stimulus interval. Only the rod response was affected; the cone response was not enhanced by continued stimulation. The effects of 12.5 μM $PbCl_2$ on rod response amplitude were complex. There was a small (< 10%) but consistent depression of rod response amplitude even when the rods were in the unenhanced state. However, the most striking effect of lead was on the enhanced response, where treatment with 12.5 μM $PbCl_2$ led to a depression of about 33%. When added before light stimulation, lead significantly decreased the degree to which the rod response could be enhanced, but never prevented enhancement entirely. Removal of lead resulted in a very large increase in the degree to which the rod response was enhanced by light, even when compared with the first, lead-free control. The cone response was unaffected by 12.5 μM $PbCl_2$.

Active Transport of Lead by Human Red Blood Cells

T.J. Simons. FEBS LETT 1984 Jul 9;172(2):250-4.

Author's abstract: Human red cells suspended in lead-citrate buffers (2.6 μM Pb^{2+}) take up much less Pb than predicted from studies of equilibrium binding of Pb to hemolysates. Pb uptake is increased by adenosine triphosphate (ATP) depletion, or by loading at 0° C. Tracer studies with ^{203}Pb indicate that the low uptake at 37° C in the presence of substrate is not due to membrane impermeability to Pb. Cold-loaded cells extrude Pb against a concentration gradient at 37° C when glucose is present. These results suggest that the cellular loading of Pb is dependent on the balance between an inward leak and an outward pump. The extrusion of Pb from the cells is possibly brought by the Ca pump.

Concentrations of Lead, Magnesium, Calcium, Zinc and Cadmium in Twenty Rabbit Tissues After Exposure to Low Lead Doses and Atherogenic Diet

M. Speich, C. Metayer, P. Arnaud, V.G. Nguyen, and H.L. Boiteau. ANN NUTR METAB 1983; 27(6): 531-41.

Authors' abstract: Four groups of six rabbits were subjected to the following diets for 25 weeks: I (controls), II (water with 9.66 μmol/l of lead), III (atherogenic), and IV (atherogenic + 9.66 μmol/l of lead). Lead, magnesium, calcium, zinc, and cadmium were then analyzed in 20 dry tissues. At the level of the arteries, veins, and skin, a tendency was observed toward increased lead concentration in rabbits of groups II and IV, elevated calcium levels in groups III and IV (a tenfold increase of calcium in the aortas), and a higher concentration of cadmium in animals of group II. There was a significant reduction in lead and magnesium concentrations in the liver of animals in groups III and IV because of fibrosis and overabundance of fatty liver cells. The lead level in the liver of animals in group II had slightly increased. Lead concentrations were higher in the kidneys and spleen in groups II and IV. Cadmium levels were significantly lower in the liver, kidneys, adrenal glands, and spleen of animals in groups III and IV,

whereas in group II they were particularly increased in the liver and kidneys. Very little significant interaction between the two diets was noted. Rabbits in groups III and IV showed notable histopathological alterations in aorta, carotid and femoral arteries, left ventricle, and liver. Extrapolation from rabbit to man would be inadvisable.

Low Lead Doses and Atherogenic Diet in Rabbits: Biochemical Results in Blood

M. Speich, C. Metayer, P. Arnaud, V.G. Nguyen, B. Bousquet, and H.L. Boiteau. ANN NUTR METAB 1983;27(6):521-30.

Authors' abstract: Changes in concentrations of blood lead, cholesterol, triacylglycerols, GOT [glutamic-oxaloacetic transaminase] and GPT [glutamic-pyruvic transaminase] enzymes, phosphorus, proteins, plasma calcium and magnesium, and erythrocyte magnesium were studied for 25 weeks in 4 groups of 6 rabbits each receiving different diets: I (controls), II (water with 9.66 μmol/l of lead), III (atherogenic), and IV (atherogenic + 9.66 μmol/l of lead). Differences observed, with respect to the diets, for lead, cholesterol, enzymes, proteins, and erythrocyte magnesium were evident from the 42nd day on. Low lead doses raised the levels of cholesterol and triacylglycerols in group II, whereas triacylglycerols were lower in the plasma of group IV in comparison with group III and were accumulated in the aorta. The elevation of enzymes in groups III and IV indicated heart and liver dysfunctions. There was a significant drop in erythrocyte magnesium in groups III and IV, which was especially marked in the latter group, with an interaction between the two diets.

The Influence of Dietary Phosphate on the Toxicity of Orally Ingested Lead in Rats

J.T. Spickett and R.R. Bell. FOOD CHEM TOXICOL 1983 Apr;21(2):157-61.

Authors' abstract: The influence of elevated dietary phosphate on the toxicity of orally ingested lead was investigated in male weanling Wistar rats. Two groups of 20 rats were fed diets containing either adequate (0.5%) or high (1.2%) levels of phosphorus (as phosphates). Half of the rats on each level of phosphorus were given 20 μg lead (as lead acetate)/g dry diet. After 8 wk, biochemical tests for lead toxicity were carried out and tissue-lead levels were measured. All of the rats given lead-supplemented diets had higher concentrations of lead in bone, brain, kidney, and liver than those given diets without added lead; but the increase was significantly greater in all tissues in the group given the 1.2% phosphorus diet. Lead supplementation increased the levels of free erythrocyte protoporphyrin and decreased the activity of δ-aminolevulinic acid dehydratase. The lead-induced increase in the level of free erythrocyte protoporphyrin was no greater in the high-phosphate group than in the low-phosphate group, but the decrease in δ-aminolevulinic acid dehydratase activity was significantly larger in the high-phosphate group. This work demonstrates that excess dietary phosphate significantly increases lead toxicity and indicates the need for continued research on the interaction between dietary factors and lead toxicity.

The Influence of Dietary Citrate on the Absorption and Retention of Orally Ingested Lead

J.T. Spickett, R.R. Bell, J. Stawell, and S. Polan. AGENTS ACTIONS 1984 Oct;15(3-4):459-62.

Authors' abstract: The influence of dietary citrate on the toxicity of orally ingested lead was investigated in male weanling mice. Twenty-four animals were divided into three equal groups. Group 1 served as controls, groups 2 and 3 were given 20 μg lead (as lead acetate) per g/diet, and group 3 also received 4% sodium citrate in the diet. After 5 weeks, blood and tissue lead levels were measured. All mice given lead-supplemented diets had higher concentrations of lead in blood, liver, kidney, brain, and bone than the control group, but the increase was significantly greater in the group given 4% sodium citrate in the diet. This work demonstrated that dietary citrate at levels that can be present in food significantly increases lead toxicity.

High Cytotoxicity and Membrane Permeability of Et_3Pb^+ in Mammalian and Plant Cells

C. Stournaras, G. Weber, H. P. Zimmermann, K.H. Doenges, and H. Faulstich. CELL BIOCHEM FUNCT 1984 Oct;2(4):213-6.

Authors' abstract: Cells of mammalian origin as well as those of higher plants appear to be very sensitive to triethyllead ion (Et_3Pb^+). Neuroblastoma cells kept in the presence of 1 μM Et_3Pb^+ lost their viability within 6 h. Growth of suspension culture cells of soybean (G. max(L.)Merr.) was inhibited by 1 μM Et_3Pb^+, and finally the cells died. Morphologically, Et_3Pb^+ caused the complete breakdown of microtubular structures in neuroblastoma cells; thus microtubules appeared to be the main target for the toxin. Although in a previous study the effect of Et_3Pb^+ on microtubules has been well documented at concentrations of 50-200 μM 1, the present study demonstrates that the formation of microtubules from pig brain tubulin is disturbed at concentrations of Et_3Pb^+ as low as 0.5 to 1 μM. We conclude from these data that Et_3Pb^+ freely permeates the plasma membranes of mammalian as well as plant cells.

Lead, Cadmium, Iron, Zinc, Copper, Manganese, Calcium and Magnesium in SPF Male Rats Exposed to a Dilution of Automotive Exhaust Gas Throughout Their Lives

M. Stupfel, A.J. Valleron, and E. Radford. SCI TOTAL ENVIRON 1983 Dec 15;32(1):65-71.

Authors' abstract: Male pathogen-free CFE albino Sprague-Dawley rats were exposed 8 h per day, 5 days per week, for 3 years to a 1/1,000 dilution of automotive exhaust gas, containing 58 ppm carbon monoxide, 0.37% carbon dioxide, 23 ppm nitrogen oxides, 2 ppm aldehydes, < 5 mg/l hydrocarbons, and 8.5 $\mu g/m^3$ lead. Lead, cadmium, iron, zinc, calcium, and magnesium were measured by atomic absorption in the femurs and tibias of the rats that died during the experiment. A comparison with two control groups revealed that the only significant difference in the elements measured in the bones was a 500% increase in lead concentration. The calculations of the correlations between the percentages of the elements in bones, the ages and the body weights of the rats, as well as cluster analysis, did not show consistent variations of the water, calcium, or magnesium concentrations nor of the other studied metals related to this increase in lead concentration. Moreover, longevity was the same in the three groups of rats, but the body weight was statistically smaller (4%) in the group exposed to the auto exhaust dilution.

Vulnerability to Lead in Protein-Deprived Suckling Rats

R. Sundstrom, N.G. Conradi, and P. Sourander. ACTA NEUROPATHOL (Berl) 1984;62(4):276-83.

From authors' abstract: Most studies on lead toxicity in the suckling rat have been performed with doses leading to growth retardation. In a previous paper (Sundstrom et al., 1983), the effects of different lead doses on normal suckling rats were described. The dose of 10 mg/kg body weight daily given on days 1-15 postpartum produced minute hemorrhagic lesions on day 15 in the cerebellum, whereas rats given 5 mg/kg body weight daily lacked microscopically discernible pathologic changes in the brain. None of these groups exhibited growth retardation. To further elucidate the association between lead encephalopathy and malnutrition, we administered lead to protein-deprived suckling rats. Protein deprivation was achieved by a diet with 50% reduction of protein content. The mothers of the pups were fed this diet from 2 weeks before conception throughout the experiment. Experimental animals were injected intraperitoneally with 5 mg or 10 mg lead nitrate/kg b.wt. daily. Littermates, injected with vehicle without lead nitrate, served as controls. Protein-deprived rats without either treatment were "external" controls. Animals were killed at 10, 15, and 20 days of age for determination of lead content in blood and brain and for light-microscopic examination. The protein-deprived rats given 10 mg/kg b.wt. daily were growth-retarded as compared with unexposed protein-deprived rats. The mortality was almost 100% at 15-20 days postpartum. At 15 days, the cerebellum of these rats showed abundant hemorrhages, and the cerebrum was also hemorrhagically discolored. Protein-deprived rats given 5 mg/kg b.wt. daily did not differ significantly from unexposed protein-deprived rats with regard to body weight gain.

Lead Poisoning in Monkeys During Pregnancy and Lactation

P. Tachon, A. Laschi, J.P. Briffaux, G. Brain, and P. Chambon. SCI TOTAL ENVIRON 1983 Sep;30:221-9.

Authors' abstract: Twenty-two female monkeys (*Macaca irus*) were given lead acetate by an intramuscular route during pregnancy and/or lactation. A high dose of lead (5 mg Pb^{2+}/kg/day) can induce abortions and death in pregnant monkeys. At a lower dose (1 mg Pb^{2+}/kg/day), the fetus can be exposed to lead via placenta and/or maternal milk. Studies with optical microscopy showed the typical renal lesions in mothers treated during pregnancy (5 months) and an erythrodiapedesis in cerebral matter of the newborn at birth.

In Vivo Study on Lead and Alcohol Interaction and the Inhibition of Erythrocyte δ-Aminolevulinic Acid Dehydratase in Man

S. Telisman, D. Prpic-Majic, and S. Kezic. SCAND J WORK ENVIRON HEALTH 1984 Aug;10(4):239-44.

Authors' abstract: The effect of alcohol (EtOH) consumption on the inhibition of erythrocyte δ-aminolevulinic acid dehydratase (ALAD) was investigated in 13 male lead workers and 7 "normal" male subjects. Lead and zinc protoporphyrin in blood and lead, and δ-aminolevulinic acid, porphobilinogen, and coproporphyrin in 24-h urine specimens were also determined. During 1 h the subjects drank 122.8 (SD 18.65) ml of an almost lead-free brandy, i.e., a dose of 11.07 mmol/kg of body weight. This dose resulted in a trend toward a parallel decrease in ALAD activity and an increase in lead in blood (PbB), both of which approached the prealcohol value 24 h after the initial alcohol ingestion. A trend toward increased lead excretion in urine (PbU) was observed on the day of alcohol ingestion, as compared with the preceding and succeeding 24-h urine specimens. However, the observed increase in PbB and PbU cannot be attributed to the small amount of lead ingested through the brandy, i.e., 7.09 (SD 1.06) nmol. The characteristic dose-effect relationship between PbB and ALAD (examined before and 1, 3, 5, and 24 h after the initial alcohol ingestion) reached the

highest correlation coefficient 3 h after the initial alcohol ingestion ($p < 0.001$). The data obtained appear to support the hypothesis of a possible role for the body lead pool and the lead-mediated influence of alcohol consumption on ALAD activity in man.

Some Actions of Lead on the Sperm and on the Male Reproductive System

J.A. Thomas and W.C. Brogan, 3d. PROG CLIN BIOL RES 1983;117:127-34.

Authors' abstract: There is evidence that lead can exert a toxic action upon the male reproductive system. Likewise, there is evidence that some of the effects that lead exerts upon other biological systems might also affect male reproductive capacity. Differences in response to the toxic actions of lead can, in part, be attributed to differences in dose, duration, method of exposure, species, and lack of comparable experimental designs. Nevertheless, a spermatotoxic and gonadotoxic effect of lead has been seen in a variety of species including man. Furthermore, lead exposure has been linked to chromosomal aberrations in workers.

In Vivo Interaction of Lead with Aminolevulinic Acid Dehydratase and Induction of a Thermolabile Factor: An Experimental Model

A. Trevisan, P. Chiesura, M. Sabbatucci, M. Raimondi, and A. Buzzo. TOXICOL LETT 1983 Aug;18(1-2):77-81.

Authors' abstract: Aminolevulinic acid dehydratase (ALA-D) activity of male albino Wistar rats was used as an experimental model for a study on the interaction of lead with biological systems. Lead at 1 mg/kg was administered intraperitoneally and the rats were killed immediately, and at 30 min, 1, 2, 3, and 4 h after treatment. It was shown that lead (Pb) interacted directly with the enzyme molecule immediately after treatment, first on the active site of zinc (Zn) and then on the thiolic groups. Induction of the so-called thermolabile factor (TF) seemed to occur later, i.e., it may only be shown from the 2nd-3rd h after treatment. The long-term persistence of lead-induced TF in the acute phase of intoxication may be the key to the interpretation of some chronic toxic effects.

Chelation of Lead by Dimercaptopropane Sulfonate and a Possible Diagnostic Use

T. Twarog and M.G. Cherian. TOXICOL APPL PHARMACOL 1984 Mar 15;72(3):550-6.

Authors' abstract: The mobilization of lead (Pb) from Pb-exposed rats was examined following administration of dimercaptopropane sulfonate (DMPS). A dose-response study showed that the highest dose of DMPS (200 μmol/kg, ip) removed Pb from kidneys, liver, and bone, but the lower doses (25 and 50 μmol/kg) chelated Pb only from the kidneys. In experiments where DMPS was repeatedly injected to Pb-exposed rats, the maximum urinary excretion of Pb was observed within 24 hr after the first injection, with little effect in subsequent injections. Discontinuation of DMPS after the first injection (at a dose of 50 μmol DMPS/kg) caused renal Pb levels to increase until further injection of DMPS, several days later, which again mobilized Pb only from the kidneys. A single oral administration of 150 μmol DMPS/kg (a dose adjusted for specific chelation from the kidney) to rats previously exposed to different doses of Pb resulted in a significant decrease of renal Pb in groups injected with more than 0.5 mg Pb/kg. A linear relationship was observed between renal Pb burden and urinary Pb excretion following chelation ($r = 0.94$, $p < 0.01$). Thus, the specific removal of Pb from the kidney by DMPS treatment suggests a potential use of DMPS, a relatively nontoxic drug, for the estimation of renal Pb burden and also for treatment of Pb poisoning. Unlike other chelating agents, DMPS can be administered orally.

The Elevation of Blood Levels of Zinc Protoporphyrin in Mice Following Whole Body Irradiation

T.L. Walden, P.S. Draganac, and W.R. Farkas. BLOOD 1984 May;63(5):1159-67.

Authors' abstract: Elevation of zinc protoporphyrin (ZPP) levels in the blood has served as an indicator of lead poisoning and iron deficiency anemia for many years. We have discovered that sublethal doses of whole body irradiation with x-rays also elevate ZPP twofold to threefold over normal levels. The ZPP level does not begin to increase until days 12-14 postirradiation and peaks between days 18 and 20 before returning to normal levels between days 28 and 35. Increasing the radiation dose delays the onset of the rise in ZPP, but does not affect the magnitude of the elevation. At lethal doses, ZPP elevation is not observed. Neither of the two previously described mechanisms that cause elevations of ZPP, namely, iron deficiency and inhibition of ferrochelatase, are responsible for the radiation-induced elevation of ZPP. The elevation of ZPP appears to be correlated with the recovery of the hematopoietic system from radiation injury.

Neurobehavioral Toxicology of the Organoleads

T.J. Walsh and H.A. Tilson. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):67-86.

Authors' abstract: Alkyl leads (R x Pb) are environmentally prevalent compounds that have been shown to

produce a variety of neurological and behavioral deficits in both laboratory animals and man. Because of the increasing commercial use of these compounds, the episodes of human poisoning, and the limited understanding of their sites and mechanisms of toxicity, the organoleads, as a class, remain potentially important environmental health hazards. Recent data indicate that the constellation of behavioral effects produced by these compounds resembles the behavioral sequelae of limbic system damage. For example, alterations in sensory responsiveness and/or behavioral reactivity and task-dependent changes in avoidance learning are observed following organolead exposure and experimental disruption of the limbic system. Furthermore, neurochemical changes induced by organoleads are regionally specific and restricted to the limbic forebrain and frontal cortex. In the present review, we summarize the toxic properties of organoleads, discuss their neurobehavioral effects, and suggest that these effects might be attributable to a disruption of the limbic forebrain.

Effects of Subacute Low Level Lead Exposure on Glucose Homeostasis

E. Whittle, R.L. Singhal, M. Collins, and P.D. Hrdina. RES COMMUN CHEM PATHOL PHARMACOL 1983 Apr;40(1):141-54.

Authors' abstract: Administration of low levels of lead (0.001, 0.005, and 0.025 μg/g/day p.o.) to neonate rats from age 3 days to 8 weeks failed to alter the activities of hepatic glucose-6-phosphatase, fructose-1,6-diphosphatase, pyruvate carboxylase, and phosphoenolpyruvate carboxykinase, the four key gluconeogenic enzymes. Administration of lead at a higher dose (0.1 μg/g/day p.o.) was also observed to produce no alterations in enzyme activity at 8 weeks. However, the higher dose did enhance the activities of fructose-1,6-diphosphatase and phosphoenolpyruvate carboxykinase at age 6 weeks. Plasma insulin and glucagon were not significantly altered by up to 0.025 μg/g exposure to lead until 8 weeks of age, although levels of these hormones appear to be slightly dose-responsive — tending towards elevated glucagon and decreased insulin levels with increasing lead dosage. At 0.1 μg/g/day, glucagon was significantly increased at 8 weeks. Blood glucose and hepatic glycogen remained unaltered. Blood, hepatic, and pancreatic lead levels were unchanged by treatment with lead up to 0.025 μg/g/day to 8 weeks of age; but there was evidence of lead accumulation in pancreatic tissue, whereas levels of the metal in the liver paralleled those in the blood. Significant increases were observed with 0.1 μg/g/day lead at 6 and 8 weeks in blood and pancreas. Data are presented which suggest that 6-week-old animals are more influenced by subacute lead exposure than are the 8-week-old animals, as reflected in some alteration of gluconeogenic enzyme activity in younger rats.

Retained Developmental Capacity of Blastocysts Transferred from Lead-Intoxicated Mice

M. Wide. TERATOLOGY 1983 Oct;28(2):293-8.

Author's abstract: Blastocysts from mice injected with an implantation-inhibiting dose of lead were transferred nonsurgically to pregnant foster mothers. This was done to obtain information about the ability of these blastocysts to implant and to develop into late fetal stages. There was no difference in the ability of lead-treated blastocysts to implant as compared with the transferred nontreated blastocysts. Nor was there any effect of the exposure to lead before implantation upon the development of the blastocysts into normal fetuses. The results indicate that the preimplantation blastocysts are protected from possible harmful influences from the lead treatment of the mothers and that the implantation failure in lead-treated mice is not due to the inability of the blastocysts to implant. A significant increase in the frequency of exencephaly was observed in fetuses derived from transplanted blastocysts as compared with those from normal pregnant mice.

On the Mechanism of Action of Lead in the Testis: In Vitro Suppression of FSH Receptors, Cyclic AMP and Steroidogenesis

J.P. Wiebe, A.I. Salhanick, and K.I. Myers. LIFE SCI 1983 Apr 25;32(17):1997-2005.

Authors' abstract: Previous evidence has shown that prenatal and neonatal exposure to low levels of Pb [lead] result in decreased FSH [follicle stimulating hormone] binding and steroidogenesis in the testes at the onset of puberty. The purpose of the present study was to determine by in vitro methods if Pb acts by interfering directly with hormone binding, cyclic AMP [adenosine monophosphate] production, and steroidogenic enzyme activity. Sertoli cells were isolated from the testes of prepubertal rats and cultured in the presence of 2.64 x 10^{-4}M of either NaAc (control) or PbAc for 1, 4, 24, 48, 96, or 144 hr. There was no reduction in FSH binding and in FSH-induced cyclic AMP after a 1- to 4-hr exposure to Pb. After a 24-hr exposure to Pb, the cells exhibited a 10%-20% decrease in FSH binding and cyclic AMP production, and after 96 hr there was a 75% decrease in these two parameters. The inhibition was greater in cells from 16-day-old rats than in those from 20-day-old rats, so that in the former, after a 144-hr exposure, the FSH-induced cyclic AMP of the Pb-exposed cells was only 3% of the amount produced by the NaAc-exposed cells (i.e., a 97% inhibition). After in vitro exposure to Pb for 48 hr, the steroidogenic activity (progesterone conversion to steroid metabolites) of Sertoli cells was significantly reduced and their steroidogenesis was no longer stimulated by FSH. A crude testicular enzyme preparation

containing 3 β-hydroxysteroid dehydrogenase (3 β-HSD) exhibited an approximately 25% reduction in activity if the assay buffer contained $PbCl_2$ instead of the equivalent in NaCl. Prolonged in vivo exposure to Pb resulted in an approximately 50% reduction in 3 β-HSD activity. This is the first indication that in the testis Pb may act directly (immediate effect) by suppressing enzyme activities, and indirectly (long-term effect) by reducing gonadotropin-receptor binding and the resultant cyclic AMP production.

Cardiac Effects of Lead

B.J. Williams, M.R. Hejtmancik, Jr., and M. Abreu. FED PROC 1983 Oct;42(13):2989-93.

Authors' abstract: Symptoms consistent with cardiac disease have been noted as part of the syndrome of lead (Pb) intoxication. All types of cardiotoxicity noted in patients have been reproduced in experimental animals exposed acutely to high concentrations of Pb or chronically exposed to lower levels. Types of cardiac effects observed include negative inotropism and electrocardiogram abnormalities, particularly conduction defects. Neonatal rats exposed to Pb via the milk of dams provided a drinking solution of lead acetate exhibit approximately four times the sensitivity to the arrhythmogenic effect of norepinephrine as adults compared with controls. Cardiotoxicity occurs after exposure as short as the first 10 postnatal days, but is not expressed until the rats are adult. Increased sensitivity to the arrhythmogenic effect of norepinephrine was seen in Pb-exposed animals in vivo and in isolated hearts from Pb-exposed animals in vitro. Norepinephrine arrhythmogenesis in vivo was attenuated by atropine or vagotomy, which indicates vagal nerve involvement. Possible mechanisms, including interference with central γ-aminobutyric acid systems, alteration of adrenergic nerve development, and Pb-Ca interaction, are discussed.

The Morphological Effects of Lead on the Developing Central Nervous System

C. Winder, L.L. Garten, and P.D. Lewis. NEUROPATHOL APPL NEUROBIOL 1983 Mar-Apr;9(2):87-108.

Authors' abstract: The pathological changes found in the central nervous system of lead-exposed humans and laboratory animals are reviewed. Data in man relate to relatively high exposure levels. In human childhood lead encephalopathy, which occurs with blood lead levels in the range 100-800 μg Pb/100 ml, edema, vacuolation, hemorrhage, and reactive glial changes appear to be secondary to microvascular lesions. No primary neuronal lesions have yet been clearly identified. Neurological signs and a pathological picture closely resembling that seen in human lead encephalopathy are obtained in young lead-exposed rats with blood lead levels above 500 μg Pb/100 ml. Edema and hemorrhage, cyst formation, reactive glial changes, and nerve cell alterations are observed consequent to changes in capillary endothelial cells and basement membranes. High-level lead exposure in rats also produces disturbances in myelinated axons and may affect neural network formation in the central nervous system. With intermediate lead levels (200-500 μg Pb/100 ml blood), vascular changes and their sequelae are not seen, but nutritional effects occur which may produce neuropathological changes. Data from recent studies on developing rats with low blood levels (up to 100 μg Pb/100 ml) appear to show effects of lead on maturing and differentiated nerve cell populations. The relevance of these changes to human subclinical lead intoxication remains to be seen. However, the overall correspondence of findings in lead-poisoned man and rat makes further investigation in this area appear necessary.

An Experimental Study of the Effects of Lead Acetate on Hearing. Cochlear Microphonics and Action Potential of the Guinea Pig

K. Yamamura, R. Kishi, N. Maehara, T. Sadamoto, and E. Uchino. TOXICOL LETT 1984 Apr;21(1):41-7.

Authors' abstract: Guinea pigs were poisoned with repeated intraperitoneal injections of 1% lead acetate. After 5 weeks, the animals were examined electrophysiologically by using cochlear microphonics (CM) and action potential (AP). The thresholds of maximum voltage of N_1 in the AP of the animals injected with a total of 100 mg lead acetate were elevated about 15 dB, and increased N_1 latency was also observed. However, no significant changes in those of CM were found. The results suggest that lead acetate not only induces damage to the peripheral nerves, but also to the cranial nerves.

Use of Pharmacological Challenges to Disclose Neurobehavioral Deficits

H. Zenick. FED PROC 1983 Dec;42(15):3191-5.

Author's abstract: Delineation of the neurotoxic effects of various environmental agents is often complicated by the considerable compensatory capacity of the central nervous system (CNS). Moreover, the degree to which such compensation occurs may be critical when one is examining dosages near the threshold for biological effect. A current approach has been to use pharmacological agents to unmask deficits that are reflected in performance on subsequent behavioral tasks. This noninvasive manipulation may also provide insight into the underlying neurochemical substrates of the CNS insult. This procedure has been successfully applied in experiments examining a wide range of compounds

(e.g., lead, mercury, acrylamide, carbon disulfide) in animals exposed during development or adulthood. Even more striking is the ability of this technique to disclose latent effects, i.e., effects that are demonstrable long after exposure has ceased. This laboratory has attempted to further elaborate the use of pharmacological probes. Utilizing a drug discrimination paradigm, we have investigated the altered amphetamine sensitivity exhibited by offspring exposed to lead early in life. This paradigm has been frequently employed in psychopharmacology and has been well validated as a tool for assessing drug response thresholds. Furthermore, additional pharmacological manipulations (agonists, depletors, blockers) can be imposed on the original drug discrimination to refine hypotheses regarding neurochemical alterations underlying the shifts observed in drug discrimination thresholds.

Lead Poisoning in Cattle: Reassessment of the Minimum Toxic Oral Dose

J. Zmudski, G.R. Bratton, C. Womac, and L. Rowe. BULL ENVIRON CONTAM TOXICOL 1983 Apr;30(4):435-41.

From the text: Under some conditions daily lead (Pb) intakes below 6 mg Pb/kg can kill calves in short periods of time. Daily Pb intakes of 2.7 mg Pb/kg can kill calves on milk diets in 20 days or less, and 5.0 mg Pb/kg/day consistently causes signs of intoxication and death in 7 days. Absorption rate of Pb is rapid and tissue depositions are high in calves on milk replacer diet. The data suggest that diet, dosing method, and dosing time must be carefully considered in evaluations of minimum toxic dose. The consistent production of seizures at these low daily Pb intakes suggests that this calf model may be valuable in the study of Pb encephalopathy. Whether daily intakes of Pb below 2.7 mg Pb/kg can cause poisoning is currently under investigation.

The Influence of Milk Diet, Grain Diet, and Method of Dosing on Lead Toxicity in Young Calves

J. Zmudzki, G.R. Bratton, C. Womac, and L.D. Rowe. TOXICOL APPL PHARMACOL 1984 Dec; 76(3): 490-7.

Authors' abstract: Twenty 2- to 3-week-old calves were fed a milk diet or a mixture of grain and hay. After acclimatization, all calves were dosed by mouth with lead acetate for 7 days, either in solution via a nursing bottle or in a gelatin capsule. At the end of the treatment period, 6 of 10 calves fed milk were either dead or showed multiple signs of Pb poisoning. All calves fed grain and hay appeared normal. Tissue Pb was significantly higher in calves on a milk diet ($p < 0.05$) compared with tissue from calves on a grain and hay diet. No significant differences were found when dosing methods were compared. These data clearly show that diet but not dosing methods greatly influenced the absorption and tissue distribution of Pb in calves. δ-Aminolevulinic acid dehydratase (ALAD) activity in blood dropped to approximately 20% of pre-Pb exposure concentrations within 24 hr after the initial dose of Pb and remained at this concentration despite continued Pb administration. Blood Pb concentrations indicate that, in this model, the Pb enters the blood rapidly and retention is prolonged. The calf model warrants further studies on absorption and metabolism.

SELECTED BIBLIOGRAPHY

Aldridge WN, Street BW. The binding of triethyllead to rat and cat hemoglobin. TOXICOL APPL PHARMACOL 1984 Apr;73(2):350-3.

*Alfano DP, Petit TL, LeBoutillier JC. Development and plasticity of the hippocampal-cholinergic system in normal and early lead exposed rats. BRAIN RES 1983 Oct;312(1):117-24.

Ashraf MH, Fosmire GJ. Effects of marginal zinc deficiency on subclinical lead toxicity in the rat neonate. J NUTR 1985 Mar;115(3):334-46.

*Atchison WD, Narahashi T. Mechanism of action of lead on neuromuscular junctions. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):267-82.

Audesirk G, Audesirk T. Chronic lead exposure reduces junctional resistance at an electrical synapse. NEUROTOXICOLOGY (Park Forest Il) 1984 Winter;5(4):1-7.

*Audesirk G, Audesirk T. Effects of chronic low level lead exposure on the physiology of individually identifiable neurons. NEUROTOXICOLOGY (Park Forest Il) 1983 Winter;4(4):13-26.

*Aungst BJ, Fung HL. Inhibition of oral lead absorption in rats by phosphate-containing products. J PHARM SCI 1983 Apr;72(4):345-8.

Bafundo KW, Baker DH, Fitzgerald PR. Lead toxicity in the chick as affected by excess copper and zinc and by Eimeria acervulina infection. POULT SCI 1984 Aug;63(8):1594-603.

*Barrett J, Livesey PJ. Lead induced alterations in maternal behavior and offspring development in the rat. NEUROBEHAV TOXICOL TERATOL 1983 Sep-Oct;5(5):557-63.

Barrett J, Livesey PJ. Low level lead effects on activity under varying stress conditions in the developing rat. PHARMACOL BIOCHEM BEHAV 1985 Jan;22(1):107-18.

Barton JC. Active transport of lead-210 by everted segments of rat duodenum. AM J PHYSIOL 1984 Aug;247(2 Pt 1):G193-8.

*Bemiller P, Kraus ER Jr. The effect of clinical and subclinical concentrations of lead on the in vitro aging of human fibroblasts. MECH AGEING DEV 1983 May;22(1):79-87.

*Berdicevsky I, Shachar M, Yannai S. Conversion of inorganic lead into a highly-toxic organic derivative by marine microorganisms. ARCH TOXICOL [Suppl] 1983;6:285-91.

*Bhattacharyya MH, Larsen RP, Furr HC, Peterson DP, Oldham RD, Moretti ES, Spaletto MI. Adsorption of Pu, Pb and Cd to mouth surfaces during oral administration to mice. HEALTH PHYS 1985 Feb;48(2):207-13.

Biddinger GR, Gloss SP. The importance of trophic transfer in the bioaccumulation of chemical contaminants in aquatic ecosystems. RESIDUE REV 1984;91:103-45.

Bjorklund H, Palmer M, Olson L, Seiger A, Hoffer B. Cerebellar Purkinje neuron hypoexcitability induced by chronic perinatal lead exposure. FED PROC 1983 Dec;42(15):3207-12.

*Blakley BR. A retrospective study of lead poisoning in cattle. VET HUM TOXICOL 1984 Dec;26(6):505-7.

Bonkowsky HL, Healey JF, Sinclair PR, Sinclair JF, Shedlofsky SI, Elder GH. Iron and the liver: acute effects of iron-loading on hepatic heme synthesis of rats. Role of decreased activity of 5-aminolevulinate dehydrase. J CLIN INVEST 1983 May;71(5):1175-82.

*Bonucci E, Barckhaus RH, Silvestrini G, Ballanti P, Di Lorenzo G. Osteoclast changes induced by lead poisoning (saturnism). APPL PATHOL 1983;1(5):241-50.

*Booze RM, Mactutus CF, Annau Z, Tilson HA. Neonatal triethyl lead neurotoxicity in rat pups: initial behavioral observations and quantification. NEUROBEHAV TOXICOL TERATOL 1983 May-Jun;5(3):367-75.

Bratton GR, Zmudzki J, Richardson EW. Lead concentrations in fresh, frozen and formalin fixed tissues from lead poisoned calves: guidelines for diagnosis. VET HUM TOXICOL 1985 Feb;27(1):7-10.

*Brownie CF, Aronson AL. Comparative effects of Ca-ethylenediaminetetraacetic acid (EDTA), ZnEDTA, and ZnCaEDTA in mobilizing lead. TOXICOL APPL PHARMACOL 1984 Sep 15;75(2):167-72.

*Bull RJ, McCauley PT, Taylor DH, Croften KM. The effects of lead on the developing central nervous system of the rat. NEUROTOXICOLOGY (Park Forest Il) 1983 Spring;4(1):1-17.

*Bushnell PJ, Levin ED. Effects of zinc deficiency on lead toxicity in rats. NEUROBEHAV TOXICOL TERATOL 1983 May-Jun;5(3):283-8.

Cadby PA, Dimitriadis E, Grant HG, Ward AD, Forbes IJ. The analysis of hematoporphyrin derivative. ADV EXP MED BIOL 1983;160:251-63.

*Abstracted

Calomiris JJ, Armstrong JL, Seidler RJ. Association of metal tolerance with multiple antibiotic resistance of bacteria isolated from drinking water. APPL ENVIRON MICROBIOL 1984 Jun;47(6):1238-42.

Carlson BL, Nielsen SW. Influence of dietary calcium on lead poisoning in mallard ducks (Anas platyrynchos). AM J VET RES 1985 Jan;46(1):276-82.

Cerklewski FL. Influence of maternal magnesium deficiency on tissue lead content of rats. J NUTR 1983 Jul;113(7):1443-7.

*Cerklewski FL. Postabsorptive effect of increased dietary zinc on toxicity and removal of tissue lead in rats. J NUTR 1984 Mar;114(3):550-4.

Chandra SV, Murthy RC, Husain T, Bansal SK. Effect of interaction of heavy metals on (Na^+ -K^+) ATPase and the uptake of 3H-DA and 3H-NA in rat brain synaptosomes. ACTA PHARMACOL TOXICOL (Copenh) 1984 Mar;54(3):210-3.

Chandra SV, Murthy RC, Saxena DK, Lal B. Effects of pre- and postnatal combined exposure to Pb and Mn on brain development in rats. IND HEALTH 1983;21(4):273-9.

Chasko GG, Hoehn TR, Howell-Heller P. Toxicity of lead shot to wild black ducks and mallards fed natural foods. BULL ENVIRON CONTAM TOXICOL 1984 Apr;32(4):417-28.

*Chiba M, Kikuchi M. The in vitro effects of zinc and manganese on δ-aminolevulinic acid dehydratase activity inhibited by lead or tin. TOXICOL APPL PHARMACOL 1984 May;73(3):388-94.

Chiba M, Kikuchi M. The in vivo effects of manganese and zinc on δ-aminolevulinic acid dehydratase activity inhibited by lead. TOXICOL LETT 1984 Feb;20(2):143-7.

Chowdhury AR, Dewan A, Gandhi DN. Toxic effect of lead on the testes of rat. BIOMED BIOCHEM ACTA 1984;43(1):95-100.

Cikrt M, Lepsi P, Tichy M. Biliary excretion of lead in rats drinking lead-containing water. TOXICOL LETT 1983 Apr;16(1-2):139-43.

*Cohn SH, Ellis KJ, Vartsky D, Wielopolski L. Applications of nuclear technologies for in vivo elemental analysis. NEUROTOXICOLOGY (Park Forest II) 1983 Fall;4(3):34-47.

Colby HD, Zulkoski JS, Johnson PB, Pope MR, Miles PR. The duration of exposure of microsomal preparations to cadmium or zinc in vitro influences the inhibition of monooxygenases. DRUG METAB DISPOS 1983 Jan-Feb;11(1):67-9.

Collins MF, Hrdina PD, Whittle E, Singhal RL. The effects of low-level lead exposure in developing rats: changes in circadian locomotor activity and hippocampal noradrenaline turnover. CAN J PHYSIOL PHARMACOL 1984 Apr;62(4):430-5.

*Columbano A, Ledda-Columbano GM, Coni PP, Vargiu M, Faa G, Pani P. Liver hyperplasia and regression after lead nitrate administration. TOXICOL PATHOL 1984;12(1):89-95.

*Cooper GP, Manalis RS. Influence of heavy metals on synaptic transmission: a review. NEUROTOXICOLOGY (Park Forest II) 1983 Winter;4(4):69-83.

Cooper GP, Manalis RS. Interactions of lead and cadmium on acetylcholine release at the frog neuromuscular junction. TOXICOL APPL PHARMACOL 1984 Jul;74(3):411-6.

*Cooper GP, Suszkiw JB, Manalis RS. Heavy metals: effects on synaptic transmission. NEUROTOXICOLOGY (Park Forest II) 1984 Fall;5(3):247-66.

Coria F, Berciano MT, Berciano J, Lafarga M. Axon membrane remodeling in the lead-induced demyelinating neuropathy of the rat. BRAIN RES 1984 Jan 23;291(2):369-72.

Cory-Slechta DA, Weiss B, Cox C. Delayed behavioral toxicity of lead with increasing exposure concentration. TOXICOL APPL PHARMACOL 1983 Dec;71(3):342-52.

Cox GS, Whitten DG. Excited state interactions of protoporphyrin IX and related porphyrins with molecular oxygen in solutions and in organized assemblies. ADV EXP MED BIOL 1983;160:279-92.

Craan AG, Nadon G, P'an AY. Lead flux through the kidney and salivary glands of rats. AM J PHYSIOL 1984 Nov;247(5 Pt 2):F773-83.

Cragg B, Rees S. Increased body:brain weight ratio in developing rats after low exposure to organic lead. EXP NEUROL 1984 Oct;86(1):113-21.

Custer TW, Franson JC, Pattee OH. Tissue lead distribution and hematologic effects in American kestrels (Falco sparverius L.) fed biologically incorporated lead. J WILDL DIS 1984 Jan;20(1):39-43.

Dallinger R, Wieser W. Molecular fractionation of Zn, Cu, Cd and Pb in the midgut gland of Helix pomatia L. COMP BIOCHEM PHYSIOL [C] 1984;79(1):125-9.

Dallinger R, Wieser W. Patterns of accumulation, distribution and liberation of Zn, Cu, Cd and Pb in different organs of the land snail Helix pomatia L. COMP BIOCHEM PHYSIOL [C] 1984;79(1):117-24.

Danielsson BR, Dencker L, Lindgren A. Transplacental movement of inorganic lead in early and late gestation in the mouse. ARCH TOXICOL 1983 Oct;54(2):97-107.

*Danielsson BR, Oskarsson A, Dencker L. Placental transfer and fetal distribution of lead in mice after treatment with dithiocarbamates. ARCH TOXICOL 1984 Mar;55(1):27-33.

*DeHaven DL, Krigman MR, Gaynor JJ, Mailman RB. The effects of lead administration during development on lithium-induced polydipsia and dopaminergic function. BRAIN RES 1984 Apr 16;297(2):297-304.

*Abstracted

*Delahunty T. Creatine kinase-BB isoenzyme in rat plasma after chronic lead intoxication. BIOCHEM BIOPHYS RES COMMUN 1984 Nov 30;125(1):192-8.

Descotes J, Evreux JC, Laschi-Locquerie A, Tachon P. Comparative effects of various lead salts on delayed hypersensitivity in mice. J APPL TOXICOL 1984 Oct;4(5):265-6.

*Dessi S, Batetta B, Laconi E, Ennas C, Pani P. Hepatic cholesterol in lead nitrate induced liver hyperplasia. CHEM BIOL INTERACT 1984 Mar;48(3):271-9.

Dobryszycka W, Zawirska B, Owczarek H, Grzebieluch M, Dzik T. Morphological and biochemical effects of long-term enteral administration of low-doses of cadmium and lead in rats. ACTA POL PHARM 1984;41(1):111-5.

Dolinsky ZS, Burright RG, Donovick PJ. Behavioral changes in mice following lead administration during several stages of development. PHYSIOL BEHAV 1983 Apr;30(4):583-9.

Donaldson WE, Leeming TK. Dietary lead: effects on hepatic fatty acid composition in chicks. TOXICOL APPL PHARMACOL 1984 Mar 30;73(1):119-23.

*Doniec J, Trojanowska B, Trzcinka-Ochocka M, Garlicka I. Effects of $Na_2CaEDTA$ on lead deposits in rabbit osseous tissue. TOXICOL LETT 1983 Oct-Nov;19(1-2):1-5.

Doyle JJ, Younger RL. Influence of ingested lead on the distribution of lead, iron, zinc, copper and manganese in bovine tissues. VET HUM TOXICOL 1984 Jun;26(3):201-4.

Duvenkamp A. Karyokinetic reactions in rat kidney proximal convoluted segment epithelium on long-term lead supply with drinking water. ACTA ANAT (Basel) 1984;119(2):121-3.

*Eaton DL, Kalman D, Garvey D, Morgan M, Omenn GS. Biological availability of lead in a paint aerosol. 2. Absorption, distribution and excretion of intratracheally instilled lead paint particles in the rat. TOXICOL LETT 1984 Sep;22(3):307-13.

*Edelstein S, Fullmer CS, Wasserman RH. Gastrointestinal absorption of lead in chicks: involvement of the cholecalciferol endocrine system. J NUTR 1984 Apr;114(4):692-700.

Edens FW, Garlich JD. Lead-induced egg production decrease in Leghorn and Japanese quail hens. POULT SCI 1983 Sep;62(9):1757-63.

Edwards MJ, Beatson J. Effects of lead and hyperthermia on prenatal brain growth of guinea pigs. TERATOLOGY 1984 Dec;30(3):413-21.

*Erickson MM, Poklis A, Gantner GE, Dickinson AW, Hillman LS. Tissue mineral levels in victims of sudden infant death syndrome. I. Toxic metals — lead and cadmium. PEDIATR RES 1983 Oct;17(10):779-84.

*Erickson MM, Poklis A, Gantner GE, Dickinson AW, Hillman LS. Tissue mineral levels in victims of sudden infant death syndrome. II. Essential minerals: copper, zinc, calcium, and magnesium. PEDIATR RES 1983 Oct;17(10):784-7.

Eskildsen J, Grandjean P. Lead exposure from lead pellets: age-related accumulation in mute swans. TOXICOL LETT 1984 May;21(2):225-9.

*Exon JH. The immunotoxicity of selected environmental chemicals, pesticides and heavy metals. PROG CLIN BIOL RES 1984;161:355-68.

*Farant JP, Wigfield DC. Comparison of the in vivo and in vitro effects of lead on the pH-activity relationship of human erythrocytic δ-aminolaevulinic acid dehydratase. BR J IND MED 1984 Aug;41(3):406-11.

Faulstich H, Stournaras C, Doenges KH, Zimmermann HP. The molecular mechanism of interaction of Et_3Pb^+ with tubulin. FEBS LETT 1984 Aug 20;174(1):128-31.

Favretto LG, Favretto L. Heavy metals at trace level in edible mussels (Mytilus galloprovincialis Lamarck) from the gulf of Trieste. Z LEBENSM UNTERS FORSCH 1984 Sep;179(3):197-200.

*Ferris NJ, Cragg BG. Organic lead and histological parameters of brain development. ACTA NEUROPATHOL (Berl) 1984;63(4):306-12.

Flora SJ, Singh S, Tandon SK. Prevention of lead intoxication by vitamin-B complex. Z GESAMTE HYG 1984 Jul;30(7):409-11.

*Flora SJ, Singh S, Tandon SK. Role of selenium in protection against lead intoxication. ACTA PHARMACOL TOXICOL (Copenh) 1983 Jul;53(1):28-32.

Fujita H, Yamamoto R, Sato K, Ikeda M. In vivo regulation of δ-aminolevulinate dehydratase activity. TOXICOL APPL PHARMACOL 1985 Jan;77(1):66-75.

Ganguly AK, Solanki KB, Mathur AK, Somasundaram K. Level of serum and renal histamine and diamine oxidase activity in lead acetate treated rats. INDIAN J PHYSIOL PHARMACOL 1984 Jan-Mar;28(1):71-2.

George JC, March GL, McKeown BA. Effects of environmental lead poisoning on the breast muscle of the Canada goose: an ultrastructural study. CYTOBIOS 1983;36(143-44):201-16.

*Gibbs PN, Gore MG, Jordan PM. Investigation of the effect of metal ions on the reactivity of thiol groups in human 5-aminolaevulinate dehydratase. BIOCHEM J 1985 Feb 1;225(3):573-80.

Gietzen DW, Woolley DE. Acetylcholinesterase activity in the brain of rat pups and dams after exposure to lead via the maternal water supply. NEUROTOXICOLOGY (Park Forest II) 1984 Fall;5(3):235-46.

*Abstracted

Girotti AW, Deziel MR. Photodynamic action of protoporphyrin on resealed erythrocyte membranes: mechanisms of release of trapped markers. ADV EXP MED BIOL 1983;160:213-25.

*Goering PL, Fowler BA. Regulation of lead inhibition of δ-aminolevulinic acid dehydratase by a low molecular weight, high affinity renal lead-binding protein. J PHARMACOL EXP THER 1984 Oct;231(1):66-71.

*Goldberg RL, Kaplan SR, Fuller GC. Effect of heavy metals on human rheumatoid synovial cell proliferation and collagen synthesis. BIOCHEM PHARMACOL 1983 Sep 15;32(18):2763-6.

*Goldstein GW. Brain capillaries: a target for inorganic lead poisoning. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):167-75.

Govoni S, Lucchi L, Battaini F, Spano PF, Trabucchi M. Chronic lead treatment affects dopaminergic control of prolactin secretion in rat pituitary. TOXICOL LETT 1984 Mar;20(3):237-41.

Govoni S, Lucchi L, Magnoni S, Spano PF, Trabucchi M. Decreased density of β-receptors in brain capillaries of lead exposed rats. DEV TOXICOL ENVIRON SCI 1983;11:521-4.

*Goyer RA. Intracellular sites of toxic metals. NEUROTOXICOLOGY (Park Forest Il) 1983 Fall;4(3):147-56.

*Guttas JJ, Carter GT, Horwitz BA. Plasma membrane protection against the acute effects of inorganic lead on the respiratory rates of intact liver cells. J TOXICOL ENVIRON HEALTH 1983 Oct-Dec;12(4-6):731-6.

Habermann E, Crowell K, Janicki P. Lead and other metals can substitute for Ca^{2+} in calmodulin. ARCH TOXICOL 1983 Sep;54(1):61-70.

Hackett PL, Kelman BJ. Availability of toxic trace metals to the conceptus. SCI TOTAL ENVIRON 1983 Jun;28:433-42.

*Haeffner EW, Zimmermann HP, Hoffmann CJ. Influence of triethyl lead on the activity of enzymes of the ascites tumor cell plasma membrane and its microviscosity. TOXICOL LETT 1984 Nov;23(2):183-8.

*Hamir AN, Sullivan ND, Handson PD. Neuropathological lesions in experimental lead toxicosis of dogs. J COMP PATHOL 1984 Apr;94(2):215-31.

*Hammond PB, Bornschein RL, Zenick H. Toxicological considerations in the assessment of lead exposure. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):53-66.

*Harada K, Miura H. Free erythrocyte protoporphyrin (FEP) and zinc protoporphyrin (ZnP) as biological parameters for lead poisoning. INT ARCH OCCUP ENVIRON HEALTH 1984;53(4):365-77.

Harry GJ, Toews AD, Krigman MR, Morell P. The effect of lead toxicity and milk deprivation of myelination in the rat. TOXICOL APPL PHARMACOL 1985 Mar 15;77(3):458-64.

*Hastings L, Zenick H, Succop P, Sun TJ, Sekeres R. Relationship between hematopoietic parameters and behavioral measures in lead-exposed rats. TOXICOL APPL PHARMACOL 1984 May;73(3):416-22.

*Hayashi M. Lead toxicity in the pregnant rat. I. The effect of high-level lead on δ-aminolevulinic acid dehydratase activity in maternal and fetal blood or tissues. ENVIRON RES 1983 Feb;30(1):152-60.

Hayashi M. Lead toxicity in the pregnant rat. II. Effects of low-level lead on δ-aminolevulinic acid dehydratase activity in maternal and fetal blood or tissue. IND HEALTH 1983;21(3):127-35.

Healy MA. Theoretical model of gastrointestinal absorption of lead. J CLIN HOSP PHARM 1984 Sep;9(3):257-61.

*Heard MJ, Chamberlain AC. Uptake of Pb by human skeleton and comparative metabolism of Pb and alkaline earth elements. HEALTH PHYS 1984 Dec;47(6):857-65.

*Heard MJ, Chamberlain AC, Sherlock JC. Uptake of lead by humans and effect of minerals and food. SCI TOTAL ENVIRON 1983 Sep;30:245-53.

Henning SJ, Leeper LL. Duodenal uptake of lead by suckling and weanling rats. BIOL NEONATE 1984;46(1):27-35.

Henning SJ, Leeper LL. Effect of cortisone on intestinal uptake of lead in the suckling rat. BIOL NEONATE 1984;46(5):249-53.

Hiasa Y, Ohshima M, Kitahori Y, Fujita T, Yuasa T, Miyashiro A. Basic lead acetate: promoting effect on the development of renal tubular cell tumors in rats treated with N-ethyl-N-hydroxyethylnitrosamine. JNCI 1983 Apr;70(4):761-5.

*Holtzman D, DeVries C, Nguyen H, Olson J, Bensch K. Maturation of resistance to lead encephalopathy: cellular and subcellular mechanisms. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):97-124.

Honda T, Nonaka S, Murayama F, Ohgami T, Shimoyama T, Yoshida H. Effects of KC-400 (polychlorinated biphenyls) on porphyrin metabolism — liver and blood porphyrin analyses in rats treated with KC-400. J DERMATOL (Tokyo) 1983 Jun;10(3):259-65.

Hopper JL. The utility of a multivariate normal model for studying familial patterns in medical and psychiatric data. AUST NZ J PSYCHIATRY 1983 Dec;17(4):342-8.

Hussein KA, Coghill SB, Milne G, Hopwood D. The uptake of lead by small intestine, colon and gallbladder of the guinea pig in vivo. HISTOCHEMISTRY 1984;81(6):591-6.

*Abstracted

Hutton M. The effects of environmental lead exposure and in vitro zinc on tissue δ-aminolevulinic acid dehydratase in urban pigeons. COMP BIOCHEM PHYSIOL [C] 1983;74(2):441-6.

*Hutton M. The role of wildlife species in the assessment of biological impact from chronic exposure to persistent chemicals. ECOTOXICOL ENVIRON SAFETY 1982 Oct;6(5):471-8.

Ireland MP. Effect of chronic and acute lead treatment in the slug Arion ater on calcium and δ-aminolaevulinic acid dehydratase activity. COMP BIOCHEM PHYSIOL [C] 1984;79(2):287-90.

*Kajimoto M, Kondo M, Niwa M, Suzuki T, Kimura H, Sasaki A, Urata G. Increase of δ-aminolevulinic acid dehydratase (ALAD) in rat erythrocytes in lead poisoning. ARCH TOXICOL 1983 Jan;52(1):1-11.

*Kalman D, Schumacher R, Covert D, Eaton DL. Biological availability of lead in a paint aerosol. 1. Physical and chemical characterization of a lead paint aerosol. TOXICOL LETT 1984 Sep;22(3):301-6.

Kant GJ, Lenox RH, Meyerhoff JL, Kenion CC, Annau Z. Effects of chronic lead exposure on release of endogenous catecholamines: a preliminary communication. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):227-34.

Kapoor SC, van Rossum GD. Effects of Pb^{2+} added in vitro on Ca^{2+} movements in isolated mitochondria and slices of rat kidney cortex. BIOCHEM PHARMACOL 1984 Jun 1;33(11):1771-8.

Karacic V, Prpic-Majic D, Skender L. Lead absorption in cows: biological indicators of ambient lead exposure. BULL ENVIRON CONTAM TOXICOL 1984 Mar;32(3):290-4.

Kasprzak KS, Hoover KL, Poirier LA. Effects of dietary calcium acetate on lead subacetate carcinogenicity in kidneys of male Sprague-Dawley rats. CARCINOGENESIS 1985 Feb;6(2):279-82.

Katti SR, Sathyanesan AG. Lead nitrate induced changes in lipid and cholesterol levels in the freshwater fish Clarias batrachus. TOXICOL LETT 1983 Oct-Nov;19(1-2):93-6.

Kawamoto JC, Overmann SR, Woolley DE, Vijayan VK. Morphometric effects of preweaning lead exposure on the hippocampal formation of adult rats. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):125-48.

Keiser JA, Vander AJ, Germain CL. Effects of lead on the secretion and disappearance of renin in rabbits. TOXICOL APPL PHARMACOL 1983 Jun 15;69(1):117-26.

Kendall RJ, Scanlon PF. The toxicology of lead shot ingestion in ringed turtle doves under conditions of cold exposure. J ENVIRON PATHOL TOXICOL ONCOL 1984 Jul;5(4-5):183-92.

Kendall RJ, Scanlon PF, Veit HP. Histologic and ultrastructural lesions of mourning doves (Zenaida macroura) poisoned by lead shot. POULT SCI 1983 Jun;62(6):952-6.

Kisseberth WC, Sundberg JP, Nyboer RW, Reynolds JD, Kasten SC, Beasley VR. Industrial lead contamination of an Illinois wildlife refuge and indigenous small mammals. J AM VET MED ASSOC 1984 Dec 1;185(11):1309-13.

Kitchen I, McDowell J, Winder C, Wilson JM. Low-level lead exposure alters morphine antinociception in neonatal rats. TOXICOL LETT 1984 Aug;22(2):119-23.

Kitchin KT. Regulation of rat hepatic δ-aminolevulinic acid synthetase and heme oxygenase activities: evidence for control by heme and against mediation by prosthetic iron. INT J BIOCHEM 1983;15(4):479-85.

Kneip TJ, Mallon RP, Harley NH. Biokinetic modelling for mammalian lead metabolism. NEUROTOXICOLOGY (Park Forest Il) 1983 Fall;4(3):189-92.

Knowlton MF, Boyle TP, Jones JR. Uptake of lead from aquatic sediment by submersed macrophytes and crayfish. ARCH ENVIRON CONTAM TOXICOL 1983;12(5):535-41.

Koga N, Hirai Y, Hasegawa T, Tomokuni K. Studies on the inhibition of erythrocyte and hepatic δ-aminolevulinic acid dehydratase activities and its restoration in mice exposed to lead. IND HEALTH 1984;22(2):83-90.

Koller LD, Exon JH, Norbury KC. Induction of humoral immunity to protein antigen without adjuvant in rats exposed to immunosuppressive chemicals. J TOXICOL ENVIRON HEALTH 1983 Aug-Sep;12(2-3):173-81.

Komulainen H, Pietarinen R, Tuomisto J. Increase in dopamine uptake in rat striatal synaptosomes after an acute in vivo administration of organic and inorganic lead. ACTA PHARMACOL TOXICOL (Copenh) 1983 May;52(5):381-9.

*Konat G. Triethyllead and cerebral development: an overview. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):87-96.

Kuettel MR, Kaplan S. Sites of lead localization in embryonic chick tissues following treatment. TERATOLOGY 1984 Feb;29(1):29-34.

Kumar S, Pant SC. Comparative effects of the sublethal poisoning of zinc, copper and lead on the gonads of the teleost Puntius conchonius ham. TOXICOL LETT 1984 Nov;23(2):189-94.

Kuttner RE, Ebata T, Schumer W. The mediated effect of endotoxin and lead upon hepatic metabolism. SURG GYNECOL OBSTET 1984 Oct;159(4):319-24.

Lach H, Srebro Z, Dziubek K, Krawczyk S, Szaroma W. The influence of mercury and lead compounds on the circadian rhythm of cytoplasmic RNA in hypothalamic neurons of mice. FOLIA HISTOCHEM CYTOCHEM (Krakow) 1983;21(3-4):231-7.

*Abstracted

*Lachant NA, Tomoda A, Tanaka KR. Inhibition of the pentose phosphate shunt by lead: a potential mechanism for hemolysis in lead poisoning. BLOOD 1984 Mar;63(3):518-24.

Landrigan PJ, Goyer RA, Clarkson TW, Sandler DP, Smith JH, Thun MJ, Wedeen RP. The work-relatedness of renal disease. ARCH ENVIRON HEALTH 1984 May-Jun;39(3):225-30.

Laschi-Loquerie A, Descotes J, Tachon P, Evreux JC. Influence of lead acetate on hypersensitivity. Experimental study. J IMMUNOPHARMACOL 1984;6(1-2):87-93.

*Ledda-Columbano GM, Columbano A, Pani P. Lead and liver cell proliferation. Effect of repeated administrations. AM J PATHOL 1983 Dec;113(3):315-20.

Lee RG, Avner DL, Berenson MM. Structure-function relationships of protoporphyrin-induced liver injury. ARCH PATHOL LAB MED 1984 Sep;108(9):744-6.

Leeming TK, Donaldson WE. Effect of dietary methionine and lysine on the toxicity of ingested lead acetate in the chick. J NUTR 1984 Nov;114(11):2155-9.

Leknes IL. Ultrastructure of bony-fish heart tissue treated with β-glycerophosphate/lead citrate or adenosine triphosphate/lead nitrate. ACTA HISTOCHEM (Jena) 1984;75(2):153-8.

Lenox RH, Kant GJ, Meyerhoff JL, Frazier JM, Annau Z. Regional brain and pituitary cyclic nucleotide response following central cholinergic stimulation in rats chronically exposed to lead. NEUROTOXICOLOGY (Park Forest II) 1984 Fall;5(3):213-25.

Levin ED, Bowman RE. The effect of pre- or postnatal lead exposure on Hamilton Search Task in monkeys. NEUROBEHAV TOXICOL TERATOL 1983 May-Jun;5(3):391-4.

Logner KR, Neathery MW, Miller WJ, Gentry RP, Blackmon DM, White FD. Lead toxicity and metabolism from lead sulfate fed to Holstein calves. J DAIRY SCI 1984 May;67(5):1007-13.

Lunetta-D'Ancona G, Russo S. Haemopoietic tissue in Perinereis cultrifera Grube: cytological identification and observations after treatment with lead. BASIC APPL HISTOCHEM 1983;27(4):303-9.

*Lutton JD, Ibraham NG, Friedland M, Levere RD. The toxic effects of heavy metals on rat bone marrow in vitro erythropoiesis: protective role of hemin and zinc. ENVIRON RES 1984 Oct;35(1):97-103.

Macdonald VW, Charache S, Hathaway PJ. Iron deficiency anemia: mitochondrial α-glycerophosphate dehydrogenase in guinea pig skeletal muscle. J LAB CLIN MED 1985 Jan;105(1):11-8.

*Malhotra KM, Murthy RC, Srivastava RS, Chandra SV. Concurrent exposure of lead and manganese to iron-deficient rats: effect on lipid peroxidation and contents of some metals in the brain. J APPL TOXICOL 1984 Feb;4(1):22-5.

Manalis RS, Cooper GP, Pomeroy SL. Effects of lead on neuromuscular transmission in the frog. BRAIN RES 1984 Feb 27;294(1):95-109.

Massaro EJ, Miller GD, Massaro TF. Multiple dose exposure effects on the tissue distribution of lead in the preweanling rat. NEUROTOXICOLOGY (Park Forest II) 1984 Fall;5(3):333-51.

*May PM, Willes MJ, Williams DR, Creighton AM. Metal binding by pharmaceuticals. Part 5. Interaction of Cd (II), Ni(II) and Pb(II) with the intracellular hydrolysis products of the anti-tumour agent ICRF 159 and its inactive homologue ICRF 192. AGENTS ACTIONS 1984 Oct;15(3-4):448-53.

*McCarren M, Eccles CU. Neonatal lead exposure in rats: I. Effects on activity and brain metals. NEUROBEHAV TOXICOL TERATOL 1983 Sep-Oct;5(5):527-31.

*McCarren M, Eccles CU. Neonatal lead exposure in rats: II. Effects on the hippocampal afterdischarge. NEUROBEHAV TOXICOL TERATOL 1983 Sep-Oct;5(5):533-40.

*McCarren M, Young GA, Eccles CU. Spectral analysis of kindled hippocampal afterdischarges in lead-treated rats. EPILEPSIA 1984 Feb;25(1):53-60.

Mele PC, Bushnell PJ, Bowman RE. Prolonged behavioral effects of early postnatal lead exposure in rhesus monkeys: fixed-interval responding and interactions with scopolamine and pentobarbital. NEUROBEHAV TOXICOL TERATOL 1984 Mar-Apr;6(2):129-35.

Missale C, Battaini F, Govoni S, Castelletti L, Spano PF, Trabucchi M. Chronic lead exposure differentially affects dopamine transport in rat striatum and nucleus accumbens. TOXICOLOGY 1984 Oct;33(1):81-90.

Mistry P, Lucier GW, Fowler BA. High-affinity lead binding proteins in rat kidney cytosol mediate cell-free nuclear translocation of lead. J PHARMACOL EXP THER 1985 Feb;232(2):462-9.

*Mittelstaedt RA, Pounds JG. Subcellular distribution of lead in cultured rat hepatocytes. ENVIRON RES 1984 Oct;35(1):188-96.

*Mobarak N, P'an AY. Lead distribution in the saliva and blood fractions of rats after intraperitoneal injections. TOXICOLOGY 1984 Jul;32(1):67-74.

*Mohammed-Brahim B, Buchet JP, Bernard A, Lauwerys R. In vitro effects of lead, mercury and cadmium on the enzymic activity of red-blood cell pyrimidine 5'-nucleotidase. TOXICOL LETT 1984 Feb;20(2):195-9.

Moingeon P, Bidart JM, Alberici GF, Boudene C, Bohuon C. In vivo modulation of muscarine receptors in rat brain by acute lead intoxication. TOXICOLOGY 1984 May 14;31(2):135-42.

*Abstracted

Molls M, Pon A, Streffer C, van Beuningen D, Zamboglou N. The effects of lead and X-rays, alone or in combination, on blastocyst formation and cell kinetics of preimplantation mouse embryos in vitro. INT J RADIAT BIOL 1983 Jan;43(1):57-69.

Muramoto S, Oki Y. Removal of some heavy metals from polluted water by water hyacinth (Eichhornia crassipes). BULL ENVIRON CONTAM TOXICOL 1983 Feb;30(2):170-7.

Mykkanen HM, Fullmer CS, Wasserman RH. Effect of phosphate on the intestinal absorption of lead (^{203}Pb) in chicks. J NUTR 1984 Jan;114(1):68-74.

Nanci A, Bai P, Warshawsky H. The effect of osmium postfixation and uranyl and lead staining on the ultrastructure of young enamel in the rat incisor. ANAT REC 1983 Sep;207(1):1-16.

Nation JR, Bourgeois AE, Clark DE. Behavioral effects of chronic lead exposure in the adult rat. PHARMACOL BIOCHEM BEHAV 1983 Jun;18(6):833-40.

Nguyen HT, Olson J, DeVries C, Savage W, Holtzman D. Scanning electron microscopic study of lead effects on cerebral astrocytes in primary culture. SCAN ELECTRON MICROSC 1982;(Pt 2):891-6.

*Nicholls DM, Kuliszewski MJ. Kidney urokinase activity following acute exposure to lead. BIOCHEM PHARMACOL 1984 Jan 15;33(2):181-6.

Nicholls DM, Teichert-Kuliszewska K, Kuliszewski MJ. The activity of membrane enzymes in homogenate fractions of rat kidney after administration of lead. TOXICOL APPL PHARMACOL 1983 Feb;67(2):193-9.

Nicholls DM, Wassenaar ML, Girgis GR, Kuliszewski MJ. Does lead exposure influence liver protein synthesis in rats? COMP BIOCHEM PHYSIOL [C] 1984;78(2):403-8.

Nicholls TJ, Handson PD. Behavioural change associated with chronic lead poisoning in working dogs. VET REC 1983 Jun 25;112(26):607.

Odenbro A, Arrhenius E. Effects of triethyllead chloride on hepatic microsomal N- and C-oxygenation of N,N-dimethylaniline in rats. TOXICOL APPL PHARMACOL 1984 Jul;74(3):357-63.

*Olson L, Bjorklund H, Henschen A, Palmer M, Hoffer B. Some toxic effects of lead, other metals and antibacterial agents on the nervous system — animal experiment models. ACTA NEUROL SCAND [Suppl] 1984;100:77-87.

Oskarsson A. Dithiocarbamate-induced redistribution and increased brain uptake of lead in rats. NEUROTOXICOLOGY (Park Forest II) 1984 Fall;5(3):283-93.

Oskarsson A. Redistribution and increased brain uptake of lead in rats after treatment with diethyldithiocarbamate. ARCH TOXICOL [Suppl] 1983;6:279-84.

Pagella PG, Bellavite O, Agozzino S, Dona GC. Pharmacological and toxicological studies on an iron succinylprotein complex (ITF282) for oral treatment of iron deficiency anemia. ARZNEIMITTELFORSCH 1984;34(9):952-8.

*Palmer MR, Bjorklund H, Taylor DA, Seiger A, Olson L, Hoffer BJ. Chronic lead exposure of the developing brain: electrophysiological abnormalities of cerebellar Purkinje neurons. NEUROTOXICOLOGY (Park Forest II) 1984 Fall;5(3):149-66.

Peter F, Strunc G. Effect of ingested lead on concentration of blood and tissue lead in rabbits. CLIN BIOCHEM 1983 Jun;16(3):202-5.

*Pickett JB, Bornstein JC. Some effects of lead at mammalian neuromuscular junction. AM J PHYSIOL 1984 Mar;246(3 Pt 1):C271-6.

Pirola BA, Borthwick IA, Srivastava G, May BK, Elliott WH. Effect of lead ions on chick-embryo liver mitochondrial δ-aminolaevulinate synthase. BIOCHEM J 1984 Sep 15;222(3):627-30.

*Poh-Fitzpatrick MB, Sklar JA, Goldsman C, Lefkowitch JH. Protoporphyrin hepatopathy. Effects of cholic acid ingestion in murine griseofulvin-induced protoporphyria. J CLIN INVEST 1983 Oct;72(4):1449-58.

Poirier LA, Theiss JC, Arnold LJ, Shimkin MB. Inhibition by magnesium and calcium acetates of lead subacetate- and nickel acetate-induced lung tumors in strain A mice. CANCER RES 1984 Apr;44(4):1520-2.

*Pounds JG. Effect of lead intoxication on calcium homeostasis and calcium-mediated cell function: a review. NEUROTOXICOLOGY (Park Forest II) 1984 Fall;5(3):295-331.

*Powers WJ Jr, Foulkes EC. Effects of lead on the renal response to extracellular volume expansion. PROC SOC EXP BIOL MED 1985 Mar;178(3):367-72.

*Prpic-Majic D, Telisman S, Kezic S. In vitro study on lead and alcohol interaction and the inhibition of erythrocyte δ-aminolevulinic acid dehydratase in man. SCAND J WORK ENVIRON HEALTH 1984 Aug;10(4):235-8.

*Purser DA, Berrill KR, Majeed SK. Effects of lead exposure on peripheral nerve in the cynomolgus monkey. BR J IND MED 1983 Nov;40(4):402-12.

*Qato MK, Maines MD. Prevention of neonatal hyperbilirubinaemia in nonhuman primates by Zn-protoporphyrin. BIOCHEM J 1985 Feb 15;226(1):51-7.

*Rader JI, Celesk EM, Peeler JT, Mahaffey KR. Effect of lead acetate on rats fed diets containing low levels of folic acid. DRUG NUTR INTERACT 1982;1(2):131-42.

*Ragan HA. The bioavailability of iron, lead and cadmium via gastrointestinal absorption: a review. SCI TOTAL ENVIRON 1983 Jun;28:317-26.

*Abstracted

Regunathan S, Sundaresan R. Pyruvate metabolism in the brain of young rats intoxicated with organic and inorganic lead. J NEUROCHEM 1984 Nov;43(5):1346-51.

Rehman S. Effects of zinc, copper, and lead toxicity on δ-aminolevulinic acid dehydratase activity. BULL ENVIRON CONTAM TOXICOL 1984 Jul;33(1):92-8.

Rehman SU, Din KU, Hasan M, Chandra O. Zinc, copper, and lead levels in blood, spinal cord and different parts of the brain in rabbit: effect of zinc-intoxication. NEUROTOXICOLOGY (Park Forest Il) 1982 Dec;3(4):195-203.

Rice DC. Behavioral deficit (delayed matching to sample) in monkeys exposed from birth to low levels of lead. TOXICOL APPL PHARMACOL 1984 Sep 15;75(2):337-45.

*Rice DC. Chronic low-lead exposure from birth produces deficits in discrimination reversal in monkeys. TOXICOL APPL PHARMACOL 1985 Feb;77(2):201-10.

Rius RA, Lucchi L, Govoni S, Trabucchi M. In vivo chronic lead exposure alters [3H]nitrendipine binding in rat striatum. BRAIN RES 1984 Nov 19;322(1):180-3.

*Roderer G, Doenges KH. Influence of trimethyl lead and inorganic lead on the in vitro assembly of microtubules from mammalian brain. NEUROTOXICOLOGY (Park Forest Il) 1983 Summer;4(2):171-80.

Ronnlund RD, Suskind RM. Iron, zinc, and other trace elements' effect on the immune response. J PEDIATR GASTROENTEROL NUTR 1983;2(Suppl 1):S172-80.

Rose HE, Quarterman J. Effects of dietary phytic acid on lead and cadmium uptake and depletion in rats. ENVIRON RES 1984 Dec;35(2):482-9.

*Rosen JF. The metabolism of lead in isolated bone cell populations: interactions between lead and calcium. TOXICOL APPL PHARMACOL 1983 Oct;71 (1):101-12.

Sadek IA. Effects of vitamin E on lead acetate, using Nyctotheroides as a single-cell model. FOLIA MORPHOL (Praha) 1984;32(3):285-7.

*Santos-Anderson RM, Tso MO, Valdes JJ, Annau Z. Chronic lead administration in neonatal rats: electron microscopy of the retina. J NEUROPATHOL EXP NEUROL 1984 Mar;43(2):175-87.

*Sasser LB, Hall GG, Bratton GR, Zmudzki J. Absorption and tissue distribution of lead in thiamin-replete and thiamin-deficient rats. J NUTR 1984 Oct;114(10):1816-25.

Sato SM, Frazier JM, Goldberg AM. Perturbation of a hippocampal zinc-binding pool after postnatal lead exposure in rats. EXP NEUROL 1984 Sep;85(3):620-30.

Saxena DK, Lal B, Murthy RC, Chandra SV. Lead induced histochemical changes in the testes of rats. IND HEALTH 1984;22(4):255-60.

Scrimshaw NS. Functional consequences of iron deficiency in human populations. J NUTR SCI VITAMINOL (Tokyo) 1984 Feb;30(1):47-63.

Shafiq-ur-Rehman. Lead-induced regional lipid peroxidation in brain. TOXICOL LETT 1984 Jun;21(3):333-7.

Shafiq-ur-Rehman, Chandra O. Regional interrelationships of zinc, copper, and lead in the brain following lead intoxication. BULL ENVIRON CONTAM TOXICOL 1984 Feb;32(2):157-65.

*Shellenberger MK. Effects of early lead exposure on neurotransmitter systems in the brain. A review with commentary. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):177-212.

Silbergeld EK. Indirectly acting neurotoxins. ACTA PSYCHIATR SCAND [Suppl] 1983;(303):16-25.

Silbergeld EK. Localization of metals: issues of importance to neurotoxicology of lead. NEUROTOXICOLOGY (Park Forest Il) 1983 Fall;4(3):193-200.

*Sillman AJ, Bolnick DA, Bosetti JB, Haynes LW, Walter AE. The effect of lead on photoreceptor response amplitude — influence of the light stimulus. EXP EYE RES 1984 Aug;39(2):183-94.

Sillman AJ, Bolnick DA, Bosetti JB, Haynes LW, Walter AE. The effects of lead and of cadmium on the mass photoreceptor potential: the dose-response relationship. NEUROTOXICOLOGY (Park Forest Il) 1982 Dec;3(4):179-94.

*Simons TJ. Active transport of lead by human red blood cells. FEBS LETT 1984 Jul 9;172(2):250-4.

*Speich M, Metayer C, Arnaud P, Nguyen VG, Boiteau HL. Concentrations of lead, magnesium, calcium, zinc and cadmium in twenty rabbit tissues after exposure to low lead doses and atherogenic diet. ANN NUTR METAB 1983;27(6):531-41.

*Speich M, Metayer C, Arnaud P, Nguyen VG, Bousquet B, Boiteau HL. Low lead doses and atherogenic diet in rabbits: biochemical results in blood. ANN NUTR METAB 1983;27(6):521-30.

*Spickett JT, Bell RR. The influence of dietary phosphate on the toxicity of orally ingested lead in rats. FOOD CHEM TOXICOL 1983 Apr;21(2):157-61.

*Spickett JT, Bell RR, Stawell J, Polan S. The influence of dietary citrate on the absorption and retention of orally ingested lead. AGENTS ACTIONS 1984 Oct;15(3-4):459-62.

Stiller D, Friedrich HJ. Ultrastructural and ultrahistochemical investigations of lead-induced intranuclear inclusion bodies in rat kidney. EXP PATHOL 1983;24(2-3):133-41.

Stinson MD, Eaton DL. Concentrations of lead, cadmium, mercury, and copper in the crayfish (Pacifasticus leniusculus) obtained from a lake receiving urban runoff. ARCH ENVIRON CONTAM TOXICOL 1983 Nov;12(6):693-9.

*Abstracted

Stone CL, Fox MR. Effects of low levels of dietary lead and iron on hepatic RNA, protein, and minerals in young Japanese quail. ENVIRON RES 1984 Apr;33(2):322-32.

*Stournaras C, Weber G, Zimmermann HP, Doenges KH, Faulstich H. High cytotoxicity and membrane permeability of Et_3Pb^+ in mammalian and plant cells. CELL BIOCHEM FUNCT 1984 Oct;2(4):213-6.

*Stupfel M, Valleron AJ, Radford E. Lead, cadmium, iron, zinc, copper, manganese, calcium and magnesium in SPF male rats exposed to a dilution of automotive exhaust gas throughout their lives. SCI TOTAL ENVIRON 1983 Dec 15;32(1):65-71.

Sundstrom R, Conradi NG, Sourander P. Low-dose lead encephalopathy in the suckling rat. ACTA NEUROPATHOL (Berl) 1983;60(1-2):1-8.

*Sundstrom R, Conradi NG, Sourander P. Vulnerability to lead in protein-deprived suckling rats. ACTA NEUROPATHOL (Berl) 1984;62(4):276-83.

Suszkiw J, Toth G, Murawsky M, Cooper GP. Effects of Pb^{2+} and Cd^{2+} on acetylcholine release and Ca^{2+} movements in synaptosomes and subcellular fractions from rat brain and Torpedo electric organ. BRAIN RES 1984 Dec 3;323(1):31-46.

Sutton RH, Wilson PD. Lead poisoning in grey-headed fruit bats (Pteropus poliocephalus). J WILDL DIS 1983 Jul;19(3):294-6.

Swarup-Mitra S, Sinha AK. Cell mediated immunity in nutritional anaemia. INDIAN J MED RES 1984 Mar;79:354-62.

*Tachon P, Laschi A, Briffaux JP, Brain G, Chambon P. Lead poisoning in monkeys during pregnancy and lactation. SCI TOTAL ENVIRON 1983 Sep;30:221-9.

Takahashi Y, Okamoto Y, Saito K. Electrocorticogram (ECoG) and auditory evoked potential (AEP) in rats intoxicated with lead acetate. IND HEALTH 1984;22(3):189-98.

Taketani S, Kohno H, Kinoshita S, Tokunaga R. The effects of lead on differentiation of the Friend leukemia cells and rat bone marrow cells. TOXICOL APPL PHARMACOL 1985 Mar 15;77(3):374-80.

Tanner DC, Lipsky MM. Effect of lead acetate on N-(4'-fluoro-4-biphenyl) acetamide-induced renal carcinogenesis in the rat. CARCINOGENESIS 1984 Sep;5(9):1109-13.

Teichert-Kuliszewska K, Nicholls DM. Rat kidney brush border enzyme activity following subchronic oral lead exposure. TOXICOL APPL PHARMACOL 1985 Feb;77(2):211-8.

*Telisman S, Prpic-Majic D, Kezic S. In vivo study on lead and alcohol interaction and the inhibition of erythrocyte δ-aminolevulinic acid dehydratase in man. SCAND J WORK ENVIRON HEALTH 1984 Aug;10(4):239-44.

*Thomas JA, Brogan WC 3d. Some actions of lead on the sperm and on the male reproductive system. PROG CLIN BIOL RES 1983;117:127-34.

Tilson HA, Mitchell CL. Neurobehavioral techniques to assess the effects of chemicals on the nervous system. ANNU REV PHARMACOL TOXICOL 1984;24:425-50.

*Trevisan A, Chiesura P, Sabbatucci M, Raimondi M, Buzzo A. In vivo interaction of lead with aminolevulinic acid dehydratase and induction of a thermolabile factor: an experimental model. TOXICOL LETT 1983 Aug;18(1-2):77-81.

*Twarog T, Cherian MG. Chelation of lead by dimercaptopropane sulfonate and a possible diagnostic use. TOXICOL APPL PHARMACOL 1984 Mar 15;72(3):550-6.

Unni LK, Caspers ML. Inhibition of bovine plasma amine oxidase by lead. BIOCHEM PHARMACOL 1984 Jul 1;33(13):2149-51.

van Rossum GD, Kapoor SC, Rabinowitz MS. Effects of inorganic lead in vitro on ion exchanges and respiratory metabolism of rat kidney cortex. ARCH TOXICOL 1985 Jan;56(3):175-81.

Verschoyle RD, Little RA. The acute toxicity of some organolead and organotin compounds in the rat, with particular reference to a gastric lesion. J APPL TOXICOL 1981 Oct;1(5):247-55.

Viau C, Bernard A, Lauwerys RR, Tulkens P, Laurent G, Maldague P. Gentamicin nephrotoxicity in cadmium, lead and mercury pretreated rats. TOXICOLOGY 1983 May;27(1):15-25.

Victery W, Miller CR, Fowler BA. Lead accumulation by rat renal brush border membrane vesicles. J PHARMACOL EXP THER 1984 Dec;231(3):589-96.

*Walden TL, Draganac PS, Farkas WR. The elevation of blood levels of zinc protoporphyrin in mice following whole body irradiation. BLOOD 1984 May;63(5):1159-67.

Walsh CT, Ryden EB. The effect of chronic ingestion of lead on gastrointestinal transit in rats. TOXICOL APPL PHARMACOL 1984 Sep 30;75(3):485-95.

Walsh TJ, McLamb RL, Tilson HA. Organometal-induced antinociception: a time- and dose-response comparison of triethyl and trimethyl lead and tin. TOXICOL APPL PHARMACOL 1984 Apr;73(2):295-9.

*Walsh TJ, Tilson HA. Neurobehavioral toxicology of the organoleads. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):67-86.

Wapnir RA, Goldstein L, Moak SA. Effects of lead on γ-glutamyl transpeptidase and (Na^+ -K^+)-adenosine triphosphatase of the small intestinal mucosa. J ENVIRON PATHOL TOXICOL ONCOL 1984 Jul;5(4-5):101-7.

*Abstracted

Warren HV, Horksy SJ, Gould CE. Quantitative analysis of zinc, copper, lead, molybdenum, bismuth, mercury and arsenic in brain and other tissues from multiple sclerosis and non-multiple sclerosis cases. SCI TOTAL ENVIRON 1983 Jul;29(1-2):163-9.

Whetsell WO Jr, Sassa S, Kappas A. Porphyrin-heme biosynthesis in organotypic cultures of mouse dorsal root ganglia. Effects of heme and lead on porphyrin synthesis and peripheral myelin. J CLIN INVEST 1984 Aug;74(2):600-7.

*Whittle E, Singhal RL, Collins M, Hrdina PD. Effects of subacute low level lead exposure on glucose homeostasis. RES COMMUN CHEM PATHOL PHARMACOL 1983 Apr;40(1):141-54.

*Wide M. Retained developmental capacity of blastocysts transferred from lead-intoxicated mice. TERATOLOGY 1983 Oct;28(2):293-8.

*Wiebe JP, Salhanick AI, Myers KI. On the mechanism of action of lead in the testis: in vitro suppression of FSH receptors, cyclic AMP and steroidogenesis. LIFE SCI 1983 Apr 25;32(17):1997-2005.

Williams BJ, Abreu ME. Cardiotoxicity of perinatal lead exposure. PROG CLIN BIOL RES 1983;140:223-35.

*Williams BJ, Hejtmancik MR Jr, Abreu M. Cardiac effects of lead. FED PROC 1983 Oct;42(13):2989-93.

*Winder C, Garten LL, Lewis PD. The morphological effects of lead on the developing central nervous system. NEUROPATHOL APPL NEUROBIOL 1983 Mar-Apr;9(2):87-108.

Winder C, Kitchen I. Lead neurotoxicity: a review of the biochemical, neurochemical and drug induced behavioural evidence. PROG NEUROBIOL 1984;22(1):59-87.

Winder C, Kitchen I, Clayton LB, Gardiner SM, Wilson JM, Lewis PD. The effect of perinatal lead administration on the ontogeny of striatal enkephalin levels in the rat. TOXICOL APPL PHARMACOL 1984 Mar 30;73(1):30-4.

Winneke G, Lilienthal H, Zimmermann U. Neurobehavioral effects of lead and cadmium. DEV TOXICOL ENVIRON SCI 1983;11:85-96.

Witek-Janusek L, Filkins JP. Relation of endotoxin structure to hypoglycemic and insulinlike actions. CIRC SHOCK 1983;11(1):23-34.

Woolley DE, Cranmer JM, eds. Neurotoxicology of lead. Reviews and recent advances. Proceedings of the Lead Neurotoxicity Symposium, September 20-21, 1982, Chicago, Illinois. NEUROTOXICOLOGY (Park Forest Il) 1984 Fall;5(3):1-361.

Woolley DE, Woolley-Efigenio ND. Specific dietary components alter the toxicity of lead exposure in the postweaning rat. PROC WEST PHARMACOL SOC 1983;26:179-83.

*Yamamura K, Kishi R, Maehara N, Sadamoto T, Uchino E. An experimental study of the effects of lead acetate on hearing. Cochlear microphonics and action potential of the guinea pig. TOXICOL LETT 1984 Apr;21(1):41-7.

Yip R, Mohandas N, Clark MR, Jain S, Shohet SB, Dallman PR. Red cell membrane stiffness in iron deficiency. BLOOD 1983 Jul;62(1):99-106.

*Zenick H. Use of pharmacological challenges to disclose neurobehavioral deficits. FED PROC 1983 Dec;42(15):3191-5.

Zimmermann HP, Doenges KH, Roderer G. Interaction of triethyl lead chloride with microtubules in vitro and in mammalian cells. EXP CELL RES 1985 Jan;156(1):140-52.

*Zmudski J, Bratton GR, Womac C, Rowe L. Lead poisoning in cattle: reassessment of the minimum toxic oral dose. BULL ENVIRON CONTAM TOXICOL 1983 Apr;30(4):435-41.

*Zmudzki J, Bratton GR, Womac C, Rowe LD. The influence of milk diet, grain diet, and method of dosing on lead toxicity in young calves. TOXICOL APPL PHARMACOL 1984 Dec;76(3):490-7.

*Abstracted

THERAPY

A Comparison of the Diminution Rates of Lead in Blood and Lead Mobilized by CaEDTA After Termination of Occupational Exposure: A Long-Term Observation in Two Lead Workers

S. Araki, K. Murata, H. Aono, S. Yanagihara, and K. Ushio. J TOXICOL CLIN TOXICOL 1983 Jul;20(5):475-86.

Authors' abstract: CaEDTA 20 mg/kg was administered weekly for 3.5 years after termination of occupational exposure to two lead workers. The diminution half-lives for lead in blood and urine lead mobilized by CaEDTA were 4.8 and 3.3 years, respectively, for subject 1 following 28 years' exposure and 3.3 and 2.0 years, respectively, for subject 2 following 26 years' exposure. The difference in the diminution rate between lead in blood and lead mobilized by CaEDTA was significant in subject 2 ($p < 0.05$).

Behavior of Lead and Zinc in Plasma, Erythrocytes, and Urine and ALAD in Erythrocytes Following Intravenous Infusion of CaEDTA in Lead Workers

S. Araki, H. Aono, M. Fukahori, and K. Tabuki. ARCH ENVIRON HEALTH 1984 Sep-Oct;39(5):363-7.

Authors' abstract: To evaluate the effect of calcium disodium ethylenediamine tetraacetate (CaEDTA) on concentrations of lead and zinc in plasma, erythrocytes, whole blood, and urine, we administered CaEDTA by intravenous infusion for 1 hr to seven lead workers with blood lead concentrations of 46-67 μg/100 g (mean, 54 μg/100 g). The plasma lead concentration (PPb) and the mobilization yield of lead in urine by CaEDTA were highest during the period between 1 and 2 hr after the infusion was started. In contrast, the lead concentration in erythrocytes (EPb) and in whole blood (BPb) remained unchanged during the 24 hr following infusion. Plasma zinc concentration (PZn) also fell rapidly following CaEDTA infusion; the decline was followed by a gradual rise in the zinc concentration in erythrocytes (EZn) without alteration in the zinc in whole blood. The mobilization yield of zinc in urine by CaEDTA (MZn) reached its highest level within 1 hr after the start of the infusion. δ-Aminolevulinic acid dehydratase (ALAD) activity in erythrocytes gradually increased for 5 hr following CaEDTA infusion. These observations suggest that (1) PPb concentration is a more sensitive indicator of the body burden of chelatable lead than is either BPb or EPb; (2) MZn is mobilized mostly from plasma during the first several hours following the start of CaEDTA infusion, and the fall in PZn concentration following infusion is compensated first by a rise in EZn concentration and then by an immediate redistribution of zinc in other organs to the blood; and (3) Pb-inhibited ALAD activity is reactivated by the increased EZn during and shortly after CaEDTA infusion.

Enzyme Replacement Therapy in Porphyrias — IV. First Successful Human Clinical Trial of δ-Aminolevulinate Dehydratase-Loaded Erythrocyte Ghosts

A.M. Batlle, N.L. Bustos, A.M. Stella, E.A. Wider, H.A. Conti, and A. Mendez. INT J BIOCHEM 1983;15(10):1261-5.

Authors' abstract: A patient with chronic lead intoxication was treated with only one course of highly purified human blood aminolevulinate dehydratase entrapped in autologous erythrocyte ghosts given intravenously. No untoward effects were observed during or after infusion. An immediate increase in the patient's erythrocyte dehydratase activity was detected 1 hr after enzyme administration, reaching its maximum and nearly normal level 2 days later; values remained unchanged for a week and slowly diminished 2 weeks after the treatment was started. Finally, recovered activity was kept practically leveled off for weeks. This novel therapeutic trial produced complete improvement, both clinical and biochemical, showing that enzyme infusion has been beneficial and can be safely and successfully used in the treatment of human lead intoxication.

The Relationship of Hyperactivity to Moderately Elevated Lead Levels

O.J. David, S.P. Hoffman, J. Clark, G. Grad, and J. Sverd. ARCH ENVIRON HEALTH 1983 Nov-Dec;38(6):341-6.

Authors' abstract: Controversy exists with respect to whether moderately elevated lead levels are toxic in certain children with various central nervous system dysfunctions. One way of addressing this controversy is to remove the lead; if the condition is ameliorated a

presumption of toxicity becomes reasonable. Such a strategy is reported herein. Children with an operationally defined central nervous system dysfunction (hyperactivity) and moderately elevated lead levels were treated with a lead chelating agent in a random allocation double-blind treatment regimen. The finding of statistically significant and obvious behavioral improvement reported by three separate evaluators (i.e., parent, teacher, and treating physician) of the child suggests that the presumption of a toxic relationship between moderately elevated lead levels and hyperactivity is supported.

Transfusion Therapy for Erythropoietic Protoporphyria

A. Dobozy, M. Csato, C. Siklosi, and N. Simon. BR J DERMATOL 1983 Nov;109(5):571-6.

Authors' abstract: Five patients with erythropoietic protoporphyria, in whom β-carotene treatment had proved unsuccessful, were treated on five or six occasions with washed, packed red blood cell transfusions. Following the transfusions, the photosensitivity and the protoporphyrin levels in the red blood cells decreased considerably. This treatment may be useful in reducing the high protoporphyrin level in patients with a rapidly deteriorating hepatic function.

Failure of Chelation Therapy in Lead Nephropathy

M.J. Germain, G.L. Braden, and J.P. Fitzgibbons. ARCH INTERN MED 1984 Dec;144(12):2419-20.

Authors' abstract: A patient with lead nephropathy and gout was treated with 3 months of edetic acid chelation. The therapy resulted in normalization of a previously abnormal result of the edetic acid lead mobilization test. Nevertheless, progressive renal insufficiency occurred. At autopsy, an increased bone lead content was documented, suggesting that the edetic acid lead mobilization test may underestimate total body lead stores and that chelation therapy may not be effective in reversing advanced lead nephropathy. Alternatively, a longer period of therapy may be necessary to remove lead stores. More studies are needed to determine the relationship between the results of the edetic acid test and bone lead stores. Methods other than the edetic acid lead mobilization test should be considered to monitor the adequacy of treatment in lead nephropathy.

Chronic Lead Poisoning in a Two-Year-Old Child. A 12-Month Follow-up Study

M. Kazacos and P. Moore. MED J AUST 1984 Mar 31;140(7):429-30.

Authors' abstract: X-ray examination of the broken arm of a 2-year-old child demonstrated the presence of lead deposits in the bone. Chelation treatment with calcium-EDTA was undertaken. The results obtained over 3 months of treatment and those obtained at the follow-up examination 12 months later are reported. The need to analyze the blood as well as the urine to obtain an accurate measure of lead concentrations is emphasized.

Effect of Mild Iron Deficiency on Infant Mental Development Scores

T. Walter, J. Kovalskys, and A. Stekel. J PEDIATR 1983 Apr;102(4):519-22.

Authors' abstract: To evaluate the effects of short-term iron therapy on developmental test scores of infants with varying stages of iron deficiency, we tested 37 infants, all 15 mo of age, with the Bayley Scales of Infant Development before and 11 days after beginning a trial of orally administered iron therapy. They were separated into three groups according to iron status: 12 controls, with normal iron nutrition; 11 with mild anemia, i.e., hemoglobin $<$ 11.0 g/dl but $>$ 8.5 g/dl; and 15 with iron deficiency without anemia, i.e., Hgb $\geq$ 11.0 g/dl but with at least one abnormal biochemical measure of iron nutrition (transferrin saturation, free erythrocyte protoporphyrin, or serum ferritin). The Mental Development Index was significantly lower in the anemic infants before treatment, as compared with that of normal controls. Improvement with iron therapy was also significant in those with anemia and in nonanemic patients with two or more biochemical indicators of iron deficiency. The rise in Mental Development Index was associated with improvement in attention span and cooperativeness. These findings suggest that mild iron deficiency has an effect on infant behavior that is rapidly reversible with iron therapy.

SELECTED BIBLIOGRAPHY

Amir M, Ahmad SH, Ansari Z, Dutta AK, Husain I. Total dose iron infusion during third trimester to iron deficient mothers. INDIAN PEDIATR 1983 May;20(5):335-9.

Anonymous. Iron deficiency and mental development. NUTR REV 1983 Aug;41(8):235-7.

Anonymous. Treatment of lead poisoning in children [editorial]. LANCET 1984 Jun 9;1(8389):1278-9.

Anonymous. Use of iron-fortified salt to combat anemia: the Indian experience. NUTR REV 1983 Oct;41(10):302-4.

Aposhian HV. DMSA and DMPS--water soluble antidotes for heavy metal poisoning. ANNU REV PHARMACOL TOXICOL 1983;23:193-215.

*Araki S, Aono H, Fukahori M, Tabuki K. Behavior of lead and zinc in plasma, erythrocytes, and urine and ALAD in erythrocytes following intravenous infusion of CaEDTA in lead workers. ARCH ENVIRON HEALTH 1984 Sep-Oct;39(5):363-7.

*Araki S, Murata K, Aono H, Yanagihara S, Ushio K. A comparison of the diminution rates of lead in blood and lead mobilized by CaEDTA after termination of occupational exposure: a long-term observation in two lead workers. J TOXICOL CLIN TOXICOL 1983 Jul;20(5):475-86.

*Batlle AM, Bustos NL, Stella AM, Wider EA, Conti HA, Mendez A. Enzyme replacement therapy in porphyrias--IV. First successful human clinical trial of δ-aminolevulinate dehydratase-loaded erythrocyte ghosts. INT J BIOCHEM 1983;15(10):1261-5.

Boscolo P, Porcelli G, Menini E, Finelli VN. EDTA plus zinc as therapy of lead intoxication: preliminary results. MED LAV 1983 Sep-Oct;74(5):370-5.

Crosby WH. The rationale for treating iron deficiency anemia. ARCH INTERN MED 1984 Mar;144(3):471-2.

*David OJ, Hoffman SP, Clark J, Grad G, Sverd J. The relationship of hyperactivity to moderately elevated lead levels. ARCH ENVIRON HEALTH 1983 Nov-Dec;38(6):341-6.

*Dobozy A, Csato M, Siklosi C, Simon N. Transfusion therapy for erythropoietic protoporphyria. BR J DERMATOL 1983 Nov;109(5):571-6.

*Germain MJ, Braden GL, Fitzgibbons JP. Failure of chelation therapy in lead nephropathy. ARCH INTERN MED 1984 Dec;144(12):2419-20.

Halliday HL, Lappin TR, McClure BG. Do all pre-term infants need iron supplements? IR MED J 1983 Oct;76(10):430-2.

*Kazacos M, Moore P. Chronic lead poisoning in a two-year-old child. A 12-month follow-up study. MED J AUST 1984 Mar 31;140(7):429-30.

Kowalczyk DF. Clinical management of lead poisoning. J AM VET MED ASSOC 1984 Apr 1;184(7):858-60.

Lundstrom U, Perkkio M, Savilahti E, Siimes M. Iron deficiency anaemia with hypoproteinaemia. ARCH DIS CHILD 1983 Jun;58(6):438-41.

May PM, Bulman RA. The present status of chelating agents in medicine. PROG MED CHEM 1983;20:225-336.

Mulligan JL, Arnold L, Sanders R, Brumwell M, Rupani M, Stelle R, Romang L, Sinnett M, Ryan P, Sirridge MS, et al. Contribution of education to cost-effective care of microcytic, hypochromic anemia. J FAM PRACT 1984 Jun;18(6):901-7.

Oppenheimer SJ, Hendrickse RG, MacFarlane SB, Moody JB, Harrison C, Alpers M, Heywood P, Vrbova H. Iron and infection in infancy--report on field studies in Papua New Guinea: II. Protocol and description of study cohort. ANN TROP PAEDIATR 1984 Sep;4(3):145-53.

Persson H. Aspects on antidote therapy in acute poisoning affecting the nervous system. ACTA NEUROL SCAND [Suppl] 1984;100:203-13.

Piomelli S, Rosen JF, Chisolm JJ Jr, Graef JW. Management of childhood lead poisoning. J PEDIATR 1984 Oct;105(4):523-32.

Sas G, Nemesanszky E, Brauer H, Scheffer K. On the therapeutic effects of trivalent and divalent iron in iron deficiency anaemia. ARZNEIMITTELFORSCH 1984;34(11):1575-9.

Schoene RB, Escourrou P, Robertson HT, Nilson KL, Parsons JR, Smith NJ. Iron repletion decreases maximal exercise lactate concentrations in female athletes with minimal iron-deficiency anemia. J LAB CLIN MED 1983 Aug;102(2):306-12.

Seshadri S, Hirode K, Naik P, Shah A, Gupta N. An effective intervention to reduce the prevalence of anaemia in children. INDIAN J MED RES 1984 Aug;80:164-73.

Simmons WK. Control of anaemia in the English-speaking Caribbean. WEST INDIAN MED J 1984 Dec;33(4):231-40.

*Abstracted

Srisupandit S, Pootrakul P, Areekul S, Neungton S, Mokkaves J, Kiriwat O, Kanokpongsukdi S. A prophylactic supplementation of iron and folate in pregnancy. SOUTHEAST ASIAN J TROP MED PUBLIC HEALTH 1983 Sep;14(3):317-23.

Trachtman L, Doucet HJ, Hazel M. Childhood lead poisoning. J LA STATE MED SOC 1984 Sep;136(9):28-32.

*Walter T, Kovalskys J, Stekel A. Effect of mild iron deficiency on infant mental development scores. J PEDIATR 1983 Apr;102(4):519-22.

Wedeen RP. Lead, mercury and cadmium nephropathy. NEUROTOXICOLOGY (Park Forest Il) 1983 Fall;4(3):134-46.

*Abstracted