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Household Pets as Monitors of Lead Exposure to Humans

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**Illinois Department of
Energy and Natural Resources**

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Acknowledgments

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Abstract

A study was conducted to determine the health effects of lead-contaminated soils in dogs, cats and children residing near a secondary lead smelter. The sample sizes were 84 dogs and 26 cats in 80 households with a total of 198 humans.

Animals living outside, exposed to soil, were more at risk of having a high blood lead concentration (BLC) than pets living inside   The strongest correlation between children and pets sharing the same household was between younger children (≤ 6 years of age) and indoor animals   The likelihood of finding someone in the household with a high BLC was significantly increased when a pet was found to have a high BLC However, the range of BLC was fairly small compared to those found in previous studies (< 5 to 28 ug/dl in pets, and 1 to 13 ug/dl in humans). Thus, the overall risk from lead contamination in this study appeared limited   The most significant changes in blood or serum biomarkers in either dogs or cats was reduced ∂-aminolevulinic acid dehydratase activity (ALAD), while free erythrocyte protoporphyrin was increased only when BLC was above 20 ug/dl.

The following conclusions were made   1) Dogs and cats in the household are more at risk than their owners of having high BLC when exposed to a similar environment   2) Soil lead concentrations should not be the major parameter used to estimate the risk of increased lead exposure to humans or their pets, since many other factors influence the bioavailability of lead, e g , soil characteristics (pH and cation exchange capacity), lead particle size and chemical form, lifestyles of both animals and humans   3) Monitoring dogs and cats would be a cost-effective way to predict risks to humans, if any, associated with a lead-contaminated environment

Executive Summary

A secondary lead smelter had been in operation in Granite City, IL for more than 80 years and was closed in 1982 Certain soils close to the smelter operation are heavily contaminated with lead, up to 5,000 ppm A study was conducted in collaboration with the US Environmental Protection Agency, Agency for Toxic Substances and Diseases Registry and the Illinois Department of Public Health to determine the health effects of exposure to lead-contaminated soils in children residing in this area Dogs and cats owned by participating families were also selected to be tested for evidence of lead exposure. A questionnaire was administered to the pet owner(s) to learn of other potential sources of lead that could bias the study. Approximately 2,600 dogs and cats were counted in the survey, while the human population approached 20,000 The sample size was 84 dogs and 26 cats in 80 households with a total of 198 humans Another 206 households without pets had a total of 629 humans who were tested

Based on the Centers for Disease Control established threshold of 10 ug/dl, only 9 % of the children tested above this level of blood lead concentration (BLC) On the contrary, 30% of the pets had a BLC above 10 ug/dl Analysis of results showed that animals living outside, exposed to dirt, were more at risk of having a high BLC than pets living inside The correlation between children and pets sharing the same household was investigated and it was found that the strongest association was between younger children ($\leq$ 6 years of age) and indoor animals There was no correlation between pets and adults The likelihood of finding someone in the household with a high BLC was significantly increased when a pet was found to have a high BLC However, the range of BLC was fairly small compared to that found in previous studies (< 5 to 28 ug/dl in pets, and 1 to 13 ug/dl in animal owners) Thus, the overall risk associated with environmental lead contamination in this study appeared limited Furthermore, no significant modification in most blood or serum biomarkers could be found in either dogs or cats The most significant change that was detected involved reduced ∂-aminolevulinic acid dehydratase activity (ALAD) A strong linear relationship was observed, even with BLC between 5-10 ug/dl. Free erythrocyte protoporphyrin was also measured and found to increase only when BLC was above 20 ug/dl

It was also shown that there was a significant relationship between BLC in pets and soil lead contamination This relationship did not appear to be true for BLC in animal owners A multiple linear regression model was built that included soil lead concentrations, the time spent outside daily by the animal, and the species No other environmental or behavioral variables were found to be significantly associated with variations in BLC. This model accounted for 37% of the total variation in BLC for that particular pet population These findings are in accordance with previous studies in human populations

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The following conclusions were made from this study.

- Dogs and cats in the household are more at risk than their owners of having high BLC when exposed to a similar environment

- Despite the increased risk from soil lead contamination, the overall BLC in humans and their pets were very low and were generally below the recently established threshold of 10 ug/dl

- Soil lead concentrations should not be the only parameter used to estimate the risk of increased lead absorption in humans or their pets, since many other factors can affect the bioavailability of lead   Instead, the concentration of lead in soil should be considered in conjunction with soil characteristics, lead particle size and chemical form, as well as behavioral features of both animals and humans

- Imposing regulatory remedial action based solely on lead concentrations in soil or dust does not appear to be legitimate   On the other hand, attempting to consider all of the environmental variables would be a difficult and expensive process   Therefore, we propose that using dogs and cats as monitors would be the most cost-effective way to assess risks to humans, if any, associated with a lead-contaminated environment

Chapter 1. Introduction

In recognition of the hazards posed by lead in the environment, the Agency for Toxic Substances and Disease Registry (ATSDR) entered into a cooperative agreement with the Illinois Department of Public Health (IDPH) to study an Illinois population exposed to lead in the environment. Their project was to evaluate human exposure to inorganic lead in the area around the NL Industries/Taracorp National Priority List (NPL or Superfund) site in Granite City, Illinois. The site, a former secondary lead smelter, has contributed to major environmental contamination from 80 years of active smelting, surface run-off, and fugitive dust emissions from contaminated on-site soils and slag piles. Soil testing by IDPH and the Illinois Environmental Protection Agency (IEPA) has detected lead contamination in the slag pile as high as 33%, in the on-site soils as high as 50,000 ppm, and in off-site soils as high as 10,000 ppm. Soil lead contamination in excess of background (100 ppm) and state standards (200 ppm) exists throughout the residential, commercial and industrial properties in Granite City, Madison, and Venice, IL that have used lead-contaminated waste from the site as fill. It is estimated that an area in excess of five square miles around the smelter site has been affected by emissions from the facility.

The present study was designed to determine the merit of using domestic animals, especially dogs and cats, as monitors/sentinels of environmental contamination. There is considerable documentation indicating that dogs might be appropriate sentinels of increased body burdens of lead and/or effects of lead in humans (Bloom *et al* , 1976; Buck, 1979; Kucera, 1988, Cattaneo *et al* , 1985; Scharding and Oehme, 1973; Koh and Babidge, 1986, Hamir *et al* , 1986, Thomas *et al* , 1976) Current research indicates that lead may have deleterious effects at levels lower than previously thought, particularly in the case of children's mental development. An estimated 5-11 million US children are considered at risk of excessive lead exposure from soil (Centers for Disease Control, 1988). The degree to which lead in soil poses a hazard and the magnitude of that hazard is not clear and may depend upon numerous socioeconomic and behavioral factors in addition to the lead content of soil. Some studies have linked children's blood lead levels to the lead levels in exterior soils and house dust (Laxen *et al* , 1987, Madhavan *et al* , 1989, Maravelias *et al* , 1989, Matte *et al* , 1989, O'Heany *et al* ,1988, Schilling and Bain, 1988). The significance of this relationship appears to vary widely, but a positive relationship was reported in all cases. These studies illustrated the interdependence between environmental sources and socioeconomic factors in determining lead body burden and consequent hazard

The premise of using animals as sentinels of potential body burdens and/or health effects from environmental toxicants was the subject of a publication by the National Research Council, under the sponsorship of ATSDR (NRC, 1991). Dogs and cats were considered to be exposed to environmental contaminants in similar ways as children in the household, although they may be more exposed to soil and dust than human adults. It was also mentioned that animal data were not as biased by socioeconomical factors as are human data

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Although cats are generally less sensitive to the toxic effects of lead than are dogs and children, they may be equally appropriate as dogs for sentinels of excessive lead in the household environment. Their grooming behavior of cleaning themselves by licking their fur tends to expose them to contaminants in house dust (Bloom *et al* , 1976), specifically, to lead in this situation. Because cats tend to inhabit the same household environment as young children, it was hypothesized that they would also be good sentinels of lead exposure to children.

Chapter 2. Material and Methods

2.1 Sampling Site

Lead contamination occurred over 55 square blocks in Granite City, Madison and Venice, Illinois. A map of the contaminated area around the smelter is presented in Figure 1

2.2 Subject Selection and Sample Collection

A census was conducted by the Illinois Department of Public Health in Granite City, Madison, and Venice, Illinois during July 1991 Questions regarding animals were included Species, sex, age and length of stay at the present address were determined The study was conducted during August through mid-October, 1991.

Subject animal selection was based on the census conducted by the Illinois Department of Public Health Only dogs and cats that had been living in Granite City for more than 60 days and were living in households from which children were sampled for blood lead determination were selected History of prior lead exposure or poisoning from any source other than soil/dust was taken into accounts by means of a questionnaire, administered at the time the animal's blood sample was taken, at one of the three veterinary clinics that participated in the study.

Blood samples were drawn from the jugular vein (cats and small dogs) or the cephalic vein (dogs) after local cleaning with 3% hydrogen peroxide, since alcohol can modify some of the test results. EDTA or heparin, lead-free tubes were used. A serum tube was also used for blood chemistry.

Approximately 2,600 pets were counted, with the human population approaching 20,000 The sample size was 84 dogs and 26 cats, while 827 humans were selected in more than 300 households. Therefore, the sampling populations in both cases were close to 4% of the total population Dogs accounted for 68 1% of the pet population surveyed and for 76 3% of the sample population These proportions were not significantly different ($p \leq 0.05$) Age and sex distribution of pets in the census versus the sampling population are given in Table 1 Significant differences are given at $p \leq 0.05$ Similar data for the human census population were not available.

2.3 Blood Lead Analyses in Pets and People

Blood lead analyses, using Graphite Furnace Atomic Absorption Spectroscopy (GFAAS) were conducted by the West Allis Industrial Toxicology Laboratory, West Allis Memorial Hospital, West Allis, WI. This laboratory was certified by both the United States Center for Disease Control (CDC) and the United States Environmental Protection Agency (USEPA) for lead analysis using rigorous QA/QC procedures Samples were shipped daily to the laboratory and analyzed immediately Only lead-free tubes were used for this test
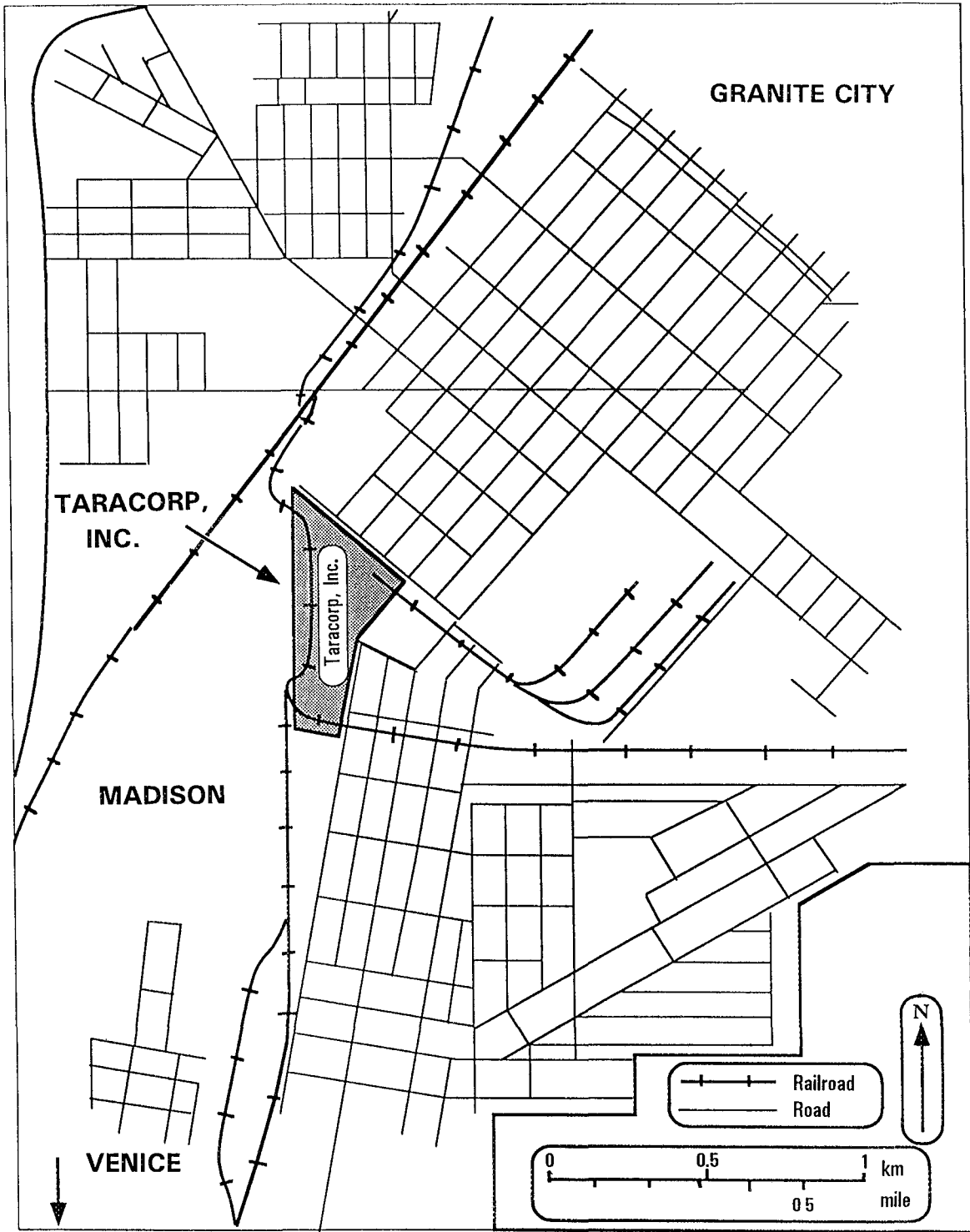
Figure 1 Map of Granite City and Madison, Madison County, Illinois showing the Taracorp, Inc. site

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Table 1: Comparison of pet census and sampling populations

	Dog (Census)	Dog (Sample)	Cat (Census)	Cat (Sample)
Juvenile (%)	27.4	14.3*	30 8	7.7*
Adult (%)	52.7	70.2*	53 2	64.6*
Elderly (%)	19 9	15.5	16 0	7.7*
Male (%)	51 2	42.9*	38 0	15.4*
Female (%)	33 1	26.2	35 6	23.1*
Neutered (%)	15 7	30.9*	26 4	61.5*
N	1765 0	84.0	827 0	26.0

* Significant difference between census and sample $p \leq 0\,05$

2.4 ∂-Aminolevulinic Acid Dehydratase Activity

Determinations of aminolevulinic acid dehydratase (ALAD) activity were done using the European Standardized Method (Berlin and Schaller, 1974) The production of porphobilinogen after adding a known amount of aminolevulinic acid to a blood sample was measured by UV spectroscopy Each sample was analyzed blind in duplicate Samples were collected in heparinized tubes, since EDTA is known to affect ALAD activity, by binding lead (Wigfield and Farant, 1981) Samples were placed on ice immediatly after they were drawn and analyzed within 4 hours To avoid contamination, all glassware was acid-washed and rinsed with glass-distilled filtered (milliQ®) water. Results were reported as nmol porphobilinogen produced/ml RBC/hour of incubation Preliminary in vitro studies were conducted to establish the optimal test conditions in dogs and cats and to determine the validity of this test in these species (Berny et al, 1992a)

2.5 Free Erythrocyte Protoporphyrin (FEP) Determination

FEP was measured using a fluorimetric method, as described by George and Duncan (1980) Each sample was analyzed in duplicate. A standard curve was established daily Only those results performed with a correlation coefficient for the standard curve above 0 99 were used Analyses were done on coded samples to avoid reading biases All glassware was acid-washed and rinsed with distilled milliQ® water Standards were prepared with erythrocyte protoporphyrin dimethyl ester (Sigma Chemicals ®) and a single batch number standard was used throughout the experiment Standard concentrations were determined using a Perkin Elmer Lambda 3 UV/VIS spectrophotometer with a millimolar absorbancy for protoporphyrin IX in hydrochloric

acid (e=241; George and Duncan, 1980) A standard curve was prepared using a Perkin-Elmer Model 203 fluoresence spectrophotometer and 20 µl of either sample, standard, or HCl blank were measured against the standard curve. Erythrocyte protoporphyrin was extracted with 1ml ethyl acetate/acetic acid (3 1) and 2 ml HCl 1 5 N Results were reported as µg FEP/dl blood

2.6 Serum Chemistry Profile

An automated method for serum chemistry profiles was used Testing was performed at the Saint Elizabeth Medical Center, Granite City, IL Quality control procedures included retesting of any sample with an unusually high or low value The following parameters were measured· sodium (Na), potassium (K), chloride (Cl), total carbon dioxide (CO_2), glucose, blood urea nitrogen (BUN), creatinine, creatine phosphokinase (CPK), lactate dehydrogenase (LDH), aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatases, total bilirubin, calcium, phosphorus, total proteins, albumin, globulin, uric acid, cholesterol concentrations, electrolyte balance and osmolality

2.7 Complete Blood Cell Counts

Complete blood cell counts (CBC) were determined with a Coulter Counter®. Red blood cell (RBC), white blood cell (WBC) counts, platelets, packed cell volume (PCV), hemoglobin concentration, and red blood cell characteristics were automatically processed Differential counts were done on slides read by trained personnel blind to the exposure status of the animal to avoid reading biases Blood samples were kept at room temperature and analyzed within 6 hours Slides were kept at room temperature until read

2.8 Basophilic Stippling

Slides were checked for basophilic stippling or any other RBC abnormality using light microscopy (x100) with an immersion lens Results were reported as positive when there was 15 or more red blood cells with basophilic stippling per 100 white blood cells

2.9 Soil, Dust, Paint and Water Lead Concentrations

The USEPA was in charge of the environmental sampling The method used was GFAAS and laboratories approved by the CDC and USEPA used stringent QA/QC procedures The dwelling interior sampling was conducted prior to the exterior sampling. A composite dust sample from various areas of the home was taken (main entrance, main room, child's bedroom) A battery operated vacuum pump with a filter cassette was used to collect dust at a standard speed, and a measured area was sampled by repeated passes over the surface area. Two water samples were taken first draw and fully flushed tap water. Outside, a composite of not less than 10 soil cores was taken from the front and the back yards. X-ray fluorescence analysis (XRF) lead readings were done on the interior paint The method has been fully described

elsewhere (Center for Disease Control, 1987)   No air-specific measurements were performed in the dwellings

2.10 Statistical Analysis

Univariate measure analyses were conducted to analyze the relationship between blood/serum biomarkers and BLC in dogs and cats   Odds ratios were computed and Mantel-Haenszel summary odds ratios were used to account for potential confounders such as age and gender   Cornfield's and exact 95% confidence intervals were determined, using the EpiInfo® package (CDC, Atlanta, GA).

Statistical analyses were conducted in several steps   The first one was to determine the correlation within people of the same household, based on age and gender groups, to pool data and facilitate further analysis. An important confounder appeared to be the time spent outside daily by animals   We, therefore, had to further divide the pet population in two subgroups   animals living mostly outside versus animals living mostly inside, based on the questionnaire data. A Pearson's matrix of correlation coefficients was obtained

The p-values and sample size are given for each categories (Table 2).

The conclusion from this table was that there was a significant correlation between males and females within the same age group, while there did not appear to be any significant correlation between other groups   Therefore, it was decided to average logBLC for males and females for each age group within each household for further analysis

Then, simple linear regression (least square method-Steel and Torrie, 1980) was used to compare blood lead concentrations in humans or animals in the same household, for each age subgroup with soil lead concentrations   To remain within the assumption of normality of residues, all blood lead concentrations had to be logarithmically transformed (positive skewness of data)   Residuals were then tested (studentized residuals) to check for normality. When outliers were noticed, the analysis was also conducted without them   Then, results with and without outliers were compared. Since there were very few outliers, no significant difference was found between those results, therefore it was decided to present data including those outliers   These analysis were conducted with the SYSTAT® package

Because of skewness of the BLC distributions and wide interindividual variation, weighted linear regression (Steel and Torrie, 1980) was used to compare blood lead concentrations (BLC) in humans and animals in the same household, for each human-age subgroup   Random, lognormally distributed values were attributed to animals with a BLC below detection limit (<5 µg/dl)   Eight 2 µg/dl blood lead intervals were determined for animals (independent variable), the mean BLC measured within each interval was used as the value for the independent variable   The number of animals used to calculate the mean was used as the weight   Animals were divided in two subgroups   those living mostly outside and their counterparts living indoor   Analyses

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Table 2: Pearson's matrix of correlation coefficients, p-values and sample size for correlation between several categories of people based on age and sex

	Male < 6yrs	Female <6yrs	Male 6-14yrs	Female 6-14yrs	Male ≥ 15yrs	Female ≥ 15yrs
Male ≤ 6yrs	1					
Female ≤ 6yrs	**0.89**	1				
	< 0 001(22)					
Male 6-14yrs	**0.30**	**0.58**	1			
	0 03(17)	*0 05(10)*				
Female 6-14yrs	**0.63**	**0.46**	**0.9**	1		
	0.03(12)	*0.23(8)*	*0 008(5)*			
Male ≥ 15yrs	**0.52**	**0.71**	**0.63**	*	1	
	0.28(5)	*0.12(4)*	*0 33(4)*	*?(2)*		
Female ≥ 15yrs	**0.66**	**0.21**	**0.4**	**0.62**	**0.75**	1
	0 09(6)	*0 69(11)*	*0.16(9)*	*0 09(4)*	*<0.001 (9)*	

Bold· correlation coefficient
Italic p value
Numbers in parentheses=sample size
* Not enough data to be computed

were conducted separately for each combination of human and animal subgroups (6 combined subgroups)

Stepwise multiple linear regression was computed using the Systat® package, to develop a model, accounting for covariates that could affect exposures, such as behavioral characteristics, type of soil cover, etc. Table 3 lists all the covariates which were tested during this process

The degree of significance selected was 0 10 for each simple linear regression coefficient   Interaction and second order models were also tested   In the final model, only variables having a significance value $p \leq 0.05$ were used (Ott, 1988)   To remain within the assumption of normality of the distributions (including residuals distribution), blood lead concentrations, as well as environmental lead concentrations (soil, dust and paint), had to be logarithmically transformed. Categorical variables were dummy-coded to be tested in the regression model

Table 3: Questionnaire information tested in the multiple linear regression model for blood lead concentration in pets

Demographic Information		Type of variable*
	Species	Categoiical (2)
	Age	Continuous
	Sex	Categorical (2)
	Neutered/Intact	Categorical (2)
	Length of stay in Gianite City	Continuous
Othei covariates		
	Free running/tied up	Categorical (2)
	Has a painted dog house/sheltei	Categorical (2)
	Time spent outside/day	Continuous
	Location where animal stays most of the time	Categorical (6)
	Soil covei	Categoiical (6)
	Dig holes	Categorical (5)
	Chewing habits	Categorical (5)
	Type of bowl used	Categorical (5)
	Type of food given	Categorical (3)
	Source of water	Categorical (3)
	Smokei at home	Categorical (5)

*number of categories given in parentheses for categorical variables

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Chapter 3. Results

3.1 Blood Lead Concentrations in Humans and Pets

The number and percentages of dogs, cats and humans with high BLC ($\geq$ 10μg/dl) or low BLC are given in Table 4

Table 4: Number and proportion of people and pets with a high BLC

	Humans w/pets*		Humans w/o pets*		Dogs		Cats	
	No	%	No	%	No	%	No	%
BLC $\geq$ 10μg/ dl	19	96 [b]	89	141 [b]	28	333 [a]	4	154 [a,b]
BLC < 10μg/dl	179	904	540	859	56	667	22	846
Total	198	100	629	100	84	100	26	100

* Humans w/ pets = people with $\geq$ 1 pet at home
Humans w/o pets = people without pets at home
superscript letters indicate groups that are not significantly different (p $\leq$ 0.05)

Roughly, 30% of the pets had high BLC while only 13% of the people sampled had high BLC The difference between peoples and pets was highly significant (Uncorrected Chi square = 19 6, p<0 001) The percentages of dogs and cats with BLC $\geq$ 10 μg/dl (33% dogs with high BLC versus 15% cats with high BLC) did not differ significantly (Chi square = 3 1 p = 0 08) Nineteen of 198 people with pets (9 6%) and 89 of 629 people without pets (14 1%) had BLC $\geq$ 10μg/dl The difference was not significant (uncorrected Chi Square = 2 75, p = 0 09) Age and sex were not associated with any significant effect (at p $\leq$ 0 05) on BLC in dogs and cats; therefore, we pooled all the animal data together in further analyses An important confounder appeared to be the time spent outside by animals. We, therefore, divided the pet population in two subgroups. animals living mostly outside versus animals living mostly inside, based on the questionnaire data. Preliminary analysis of odds ratios did not show any significant difference between species as far as blood lead concentrations were concerned

BLC were not normally distributed either in humans or in animals, but were found to follow a lognormal distribution A matrix of Pearson's correlation coefficients was obtained for all human subgroups (based on sex and age) Table 2 summarizes the correlation coefficients, p-values and sample size in each case. Based on this analysis, it was decided to pool male and female data and analyze separately each age group (less than 6 years old, 6-14 years old, 15 and older) For each household, data were averaged

for people in the same age group. None of the pet's owners had to be removed from the study because of increased likelihood of lead exposure from occupational or leisure activities. Paint lead levels were not very high (< 6 $\mu g/cm^2$) in the subpopulation of people with pets Three households were found with paint lead concentrations above 6 $\mu g/cm^2$ They were removed from the analysis. Figures 2 and 3 show BLC distribution in people with or without a pet

Figure 2: Blood lead concentration distribution (ug/dl) in two populations: people with pets and people without pets at home
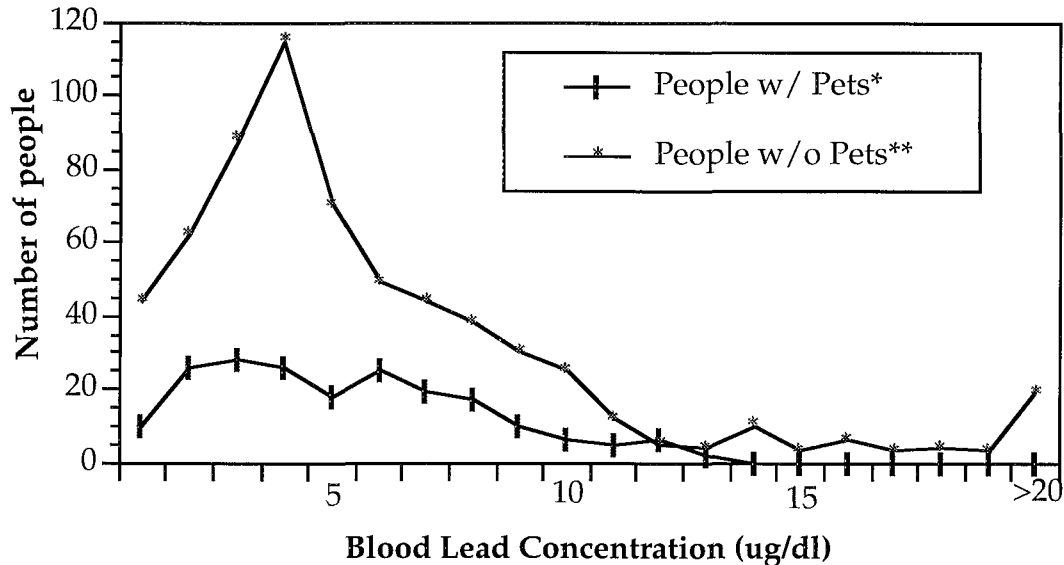
* People with ≥ 1 pet at home (198 persons)
** People without household pets (629 persons)

Figure 3: Blood lead concentration distribution (ug/dl) in the population of people with pets and in three different age groups

* People with ≥ 1 pet at home (198 persons)

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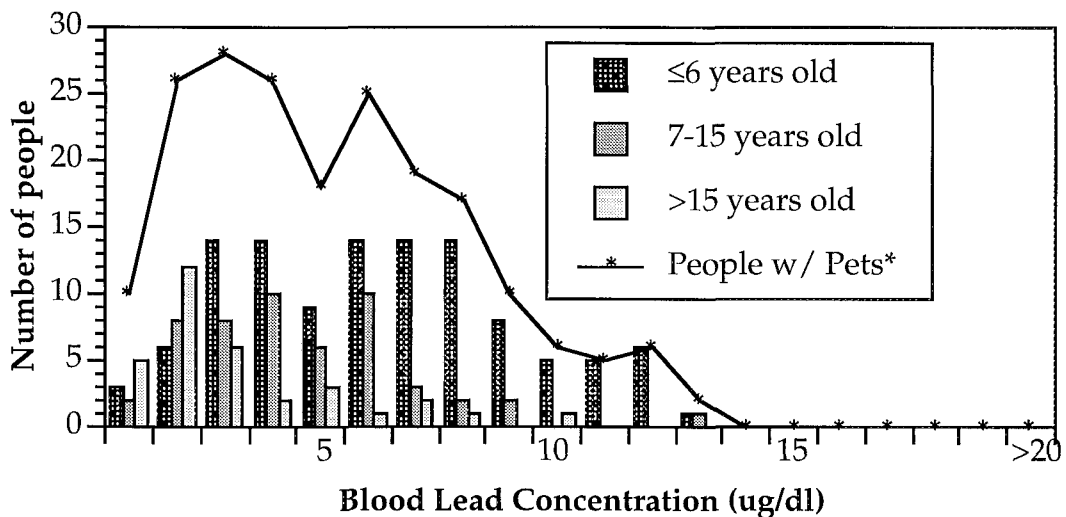
Figure 3 shows BLC distribution per age group, for people with household pets

No significant difference (p = 0 05) was found between people with pets and people without pets, as far as BLC (mean log BLC in people with pets 0 887 ±0 221; without pets 0.668 ± 0 328)

3.2 ALAD Activity in Dogs and Cats

The ALAD activities in dogs and cats are given in Figures 4-6   Linear regression slopes as well as correlation coefficients, coefficients of determination and p-values are presented in Table 5

Figure 4: Relationship between Aminolevulinic acid dehydrates (ALAD) activity and blood lead concentrations (BLC) in younger dogs and cats
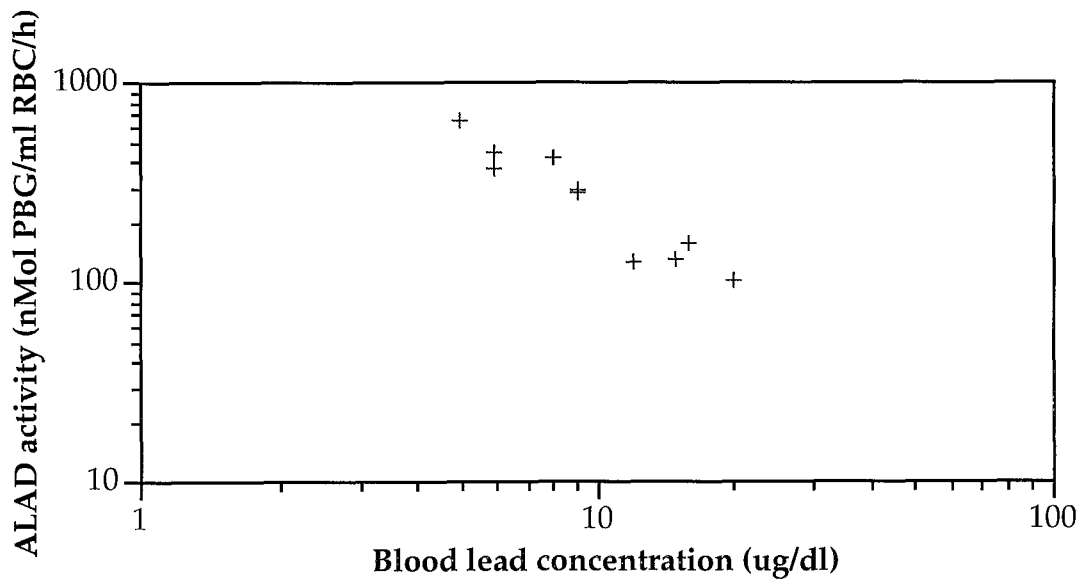
Figure 5: Relationship between Aminolevulinic acid dehydratase (ALAD) activity and blood lead concentrations (BLC) in adult dogs and cats
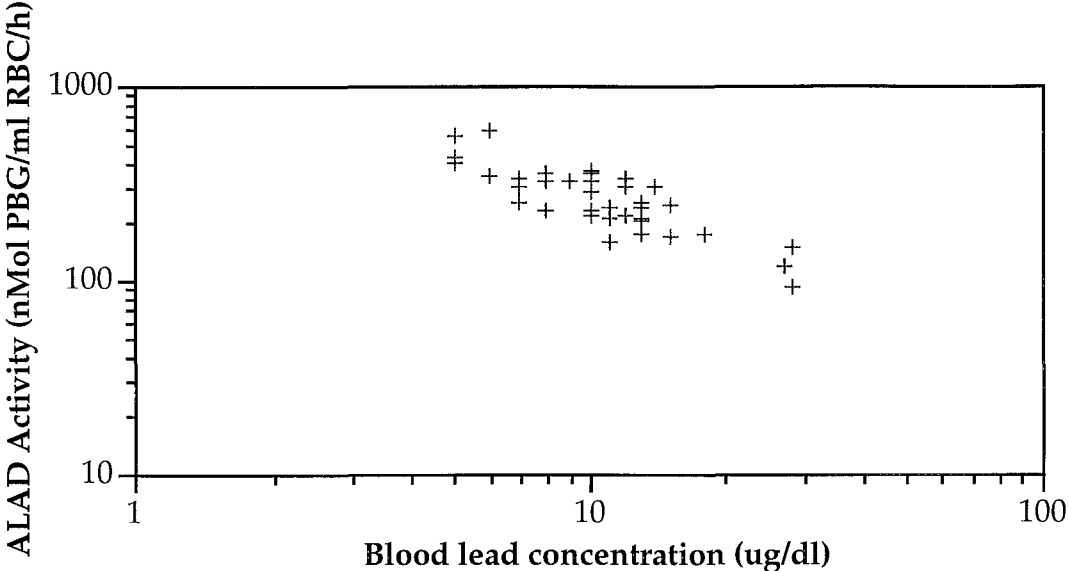
Figure 6: Relationship between Aminolevulinic acid dehydratase (ALAD) activity and blood lead concentrations (BLC) in elderly dogs and cats
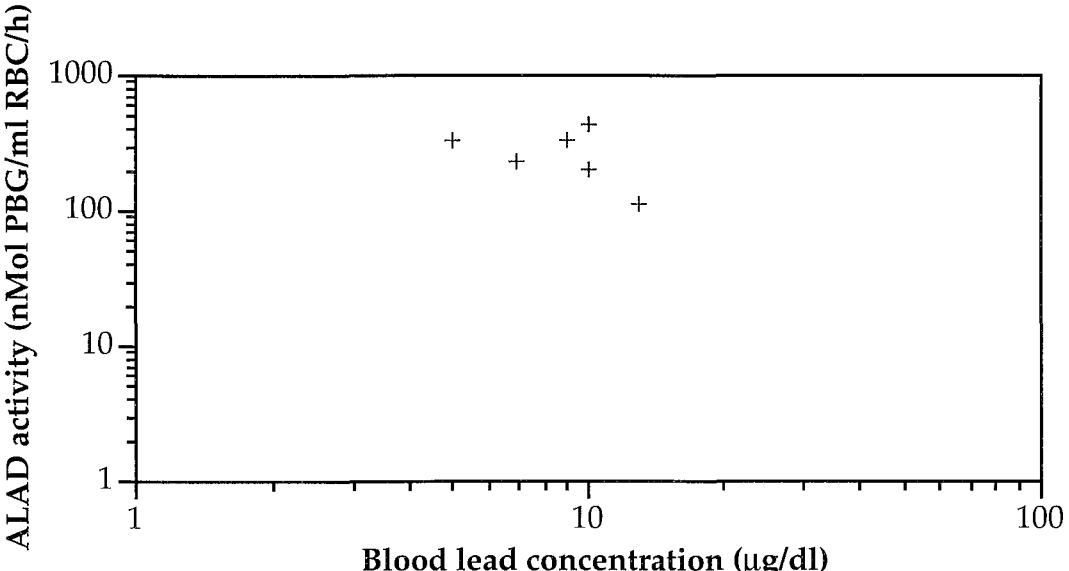
Table 5: Linear regression for log (∂-aminolevulinic acid dehydratase activity) vs log (blood lead concentration) in young, adult and elderly dogs and cats

Category	ß	r	p-value	sample size
Juvenile	-1 32 ± 0 19	-0 95	<0 001	10
Adults	-0 73 ± 0 07	-0 86	<0.001	45
Elderly	-0 63 ± 0.20	-0 74	<0 001	6

There is no prior report on ALAD activity in cats In a preliminary study, with *in vitro* lead contamination, no significant difference was found between dogs and cats (Berny et al, 1992a) It seemed reasonable to analyze data from both species together and separately to determine whether or not species was a confounding factor for ALAD inhibition. No significant species difference was found at p<0 05 between slopes and correlation coefficients

Age is known to affect the response of ALAD to lead, therefore the results are presented separately for each age group ALAD activity ranged from 800 to 80 nMol Porphobilinogen/ml RBC/hour of incubation The overall regression coefficient was -0 78 in dogs (p<0 001), in the 61 animals with a BLC above the minimum detection limit.

3.3 FEP Concentration in Dogs and Cats

The relationship between FEP concentrations and BLC is presented in Figure 7

A linear regression analysis was performed, using only those animals with a BLC ≥ 5 µg/dl and a log transformation of FEP and BLC values to fit the normality assumption The coefficient of determination (r^2) was only 0 25 (p<0.001) Statistical analysis performed with adjustment for age and sex in each species did not reveal any significant difference among any of these groups

3.4 Serum Chemistry Profile

Some species differences in serum chemistry were observed. A few marginally significant changes were observed for some serum values lower albumin concentration in cats with lower BLC, higher albumin/globulin ratio in dogs with lower BLC All the values remained within normal limits Results are presented in Table 6

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Figure 7: Relationship between free erythrocyte protoporphyrin (FEP) and blood lead concentrations in 54 dogs and 7 cats
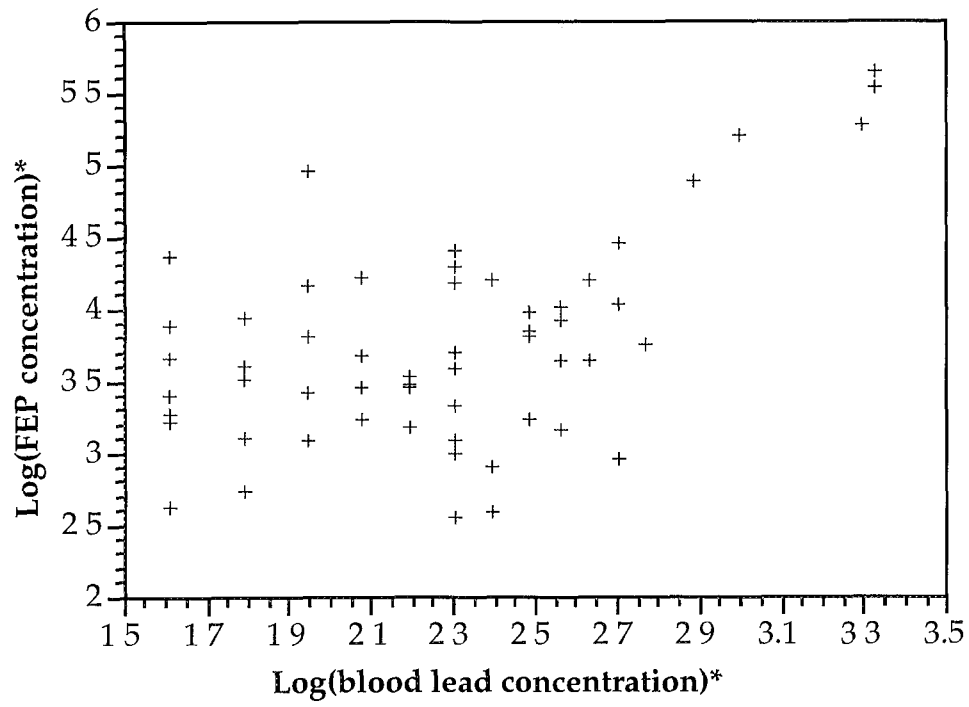
* Concentration in µg/dl

Table 6: Serum biochemical values for dogs and cats with blood lead concentration ≥ or < 10 µg/dl

	Dog		Cat	
	Pb ≥ 10 µg/dl	Pb < 10 µg/dl	Pb ≥ 10 µg/dl	Pb < 10 µg/dl
Glucose mg/dl	83.5 ± 13.6	83.2 ± 13.8	91 5 ± 0 6	89 5 ± 2 1
CPK* IU/l	141	169	170 5	151
LDH* IU/l	168	190	204	194 5
Total Bilirubin* mg/dl	0.3	0.2	0 3	0 3
Calcium mg/dl	9.8 ± 0.4	9.7 ± 0.6	9 5 ± 0 2	9 3 ± 0 5
Phosphorus mg/dl	3 95 ± 0.8	4.59 ± 1 6	4 5 ± 0 4	4 6 ± 0 7
Na mEq/l	146.5 ± 1.9	146.5 ± 2.5	152 5 ± 3 0	152 0 ± 2 6
K mEq/l	4.6 ± 0 3	4.7 ± 0.3	4 3 ± 0 1	4 3 ± 0 4
Cl mEq/l	111.4 ± 3 5	111.9 ± 4.4	117 5 ± 3 0	118 4 ± 5 2
Total CO2 mEq/l	20.5 ± 2 9	20.1 ± 2.7	18 1 ± 0 9	17 7 ± 1 5
Protein g/dl	6 8 ± 0.7	6.6 ± 0.6	7 2 ± 0 3	7 1 ± 0 4
Albumin g/dl	3 6 ± 0.3	3.7 ± 0.5	3 9 ± 0 1	3 7 ± 0 4**
Globulin g/dl	3.2 ± 0.8	2.9 ± 0.6	3 3 ± 0 3	3 4 ± 0 5
A/G Ratio	1.2 ± 0.3	1.4 ± 0.7**	1 2 ± 0 1	1 1 ± 0 2
Uric Acid mg/dl	0.32 ± 0.14	0.28 ± 0 18	0 25 ± 0 06	0 24 ± 0 11
Cholesterol mg/dl	176 5 ± 49 3	190.4 ± 50.4	110 5 ± 13 2	118 5 ± 32 2
Elec Balance mEq/l	18.46 ± 3.15	18.78 ± 3.75	22 00 ± 2 77	20 87 ± 6 21

* Because of skewness of the distribution, only medians are reported
** p<0 10

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3.5 Complete Blood Cell Counts

Results of hemoglobin (Hgb) measurements are presented in Tables 7-9

Table 7: Mean blood urea nitrogen (BUN), creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatases (Alk Phos), hemoglobin (Hgb), hematocrit (PCV), red blood cell counts (RBC) and white blood cell counts (WBC) in dogs and cats

Parameter	Units	Animals			
		Dog	*SD*	**Cat**	*SD*
BUN	mg/dl	**18.2**	*6 6*	**26.1**	*5.0*
Creatinine	mg/dl	**1.1**	*0.2*	**1.5**	*0.4*
AST	IU/l	**30.0**	-	**27.5**	-
ALT	IU/l	**37.0**	-	**39.0**	-
Alk Phos	IU/l	**40.0**	-	**32.0**	-
Hgb	g/dl	**15.8**	*2 1*	**12.9**	*2.4*
PCV	%	**44.5**	*5 7*	**37.2**	*6 5*
RBC	million/ml	**6.6**	*0.8*	**7.5**	*1 1*
WBC	thousand/ ml	**12.6**	*3.9*	**14.4**	*4.9*

• Because of skewed distribution, **AST, ALT, Alk Phos** reported as **medians** No standard deviation reported

Table 8: Association of blood lead concentrations (BLC) $\geq$ 10 μg/dl or < 10 μg/dl with blood urea nitrogen (BUN), creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatases (Alk Phos), hemoglobin (Hgb), hematocrit (PCV), red blood cell counts (RBC) white blood cell counts (WBC) and ∂-aminolevulinic acid dehydratase activity (ALAD) in dogs

Parameter	Units	Pb < 10 μg/dl (n = 56)	SD	Pb $\geq$ 10 μg/dl (n = 28)	SD
			Blood lead concentration		
BUN	mg/dl	17.9	7 1	18.7	5 5
Creatinine	mg/dl	1.1	0 3	1.1	0 2
AST*	IU/l	30.0	16-93	31.0	21-51
ALT*	IU/l	37.0	21-165	39.0	16-191
Alk Phos*	IU/l	32.5	11-313	42.0	12-97
Hgb	g/dl	16.1	2 1	15 3	2 0
PCV	%	45.1	5 6	43.5	5 4
RBC	10^6/ml	6 7	0 8	6.5	0 7
WBC	10^3/ml	11.8	3 0	13.8**	5 4
Log(ALAD)*[1]		439.6	229 3-702 8	215.7	78 7-432 0

*Because of skewed distributions, AST, ALT, Alk Phos, ALAD are reported as medians and ranges (in SD column)

** significant difference between high and low BLC group p<0 10

[1] ALAD in nmol porphobilinogen/ml RBC x incubation time (h)

Table 9: Association of blood lead concentrations (BLC) ≥ 10 μg/dl or < 10 μg/dl with blood urea nitrogen (BUN), creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatases (Alk Phos), hemoglobin (Hgb), hematocrit (PCV), red blood cell counts (RBC), white blood cell counts (WBC) and ∂-aminolevulinic acid dehydratase activity (ALAD) in cats

| Parameter | Units | Blood lead concentration | | | |
		Pb < 10 μg/dl (n = 22)	SD	Pb ≥ 10 μg/dl (n = 4)	SD
BUN	mg/dl	26.0	5 3	26.5	2 4
Creatinine	mg/dl	1.5	0 4	1.6	0 1
AST*	IU/l	27 5	17-43	27 5	24-31
ALT*	IU/l	52.0	31-110	39 0	32-57
Alk Phos*	IU/l	32.5	10-101	40 0	28-47
Hgb	g/dl	12.9	2 6	12 4	0 7
PCV	%	37.1	7 1	37 7	2 7
RBC	10^6/ml	7.5	1 1	7 2	0 3
WBC	10^3/ml	12.9	4 8	14.7**	6 4
Log(ALAD)*[1]		191	157-358	467	342-771

*Because of skewed distributions, AST, ALT, Alk Phos and ALAD are reported as medians and ranges (in SD columm)

** significant difference between high and low BLC group p<0 10

[1] ALAD in nmol porphobilinogen/ml RBC x incubation time (h)

The mean Hgb was 15 84 g/dl in dogs and 12 85 g/dl in cats These values are similar to reported normal values (Fraser et al, 1991). Changes in Hgb concentration seemed to be associated with BLC, in adult dogs, since a significant difference between cases and non cases was observed in this group This association was not observed in any other age or sex group in dogs or cats

Except for some expected species differences, no significant difference was found between animals with a high BLC and animals with a low BLC for most blood biomarkers (Table 7-9)

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WBC results are presented in Tables 7-9 The WBC count was significantly higher in cats (14,400/ml blood) than in dogs (12,560/ml blood) WBC counts were significantly higher (p<0 10) in cases (i e , animal or human with BLC ≥ 10 ug/dL) than non-cases (i e , BLC < 10 ug/dL). The same trend was observed for each age and sex group of dogs, and each sex group of cats (Figure 8), although the difference was not always significant

Figure 8: Association of age, sex and blood lead concentrations (BLC) with white blood cell counts (WBC) in 84 dogs and 26 cats
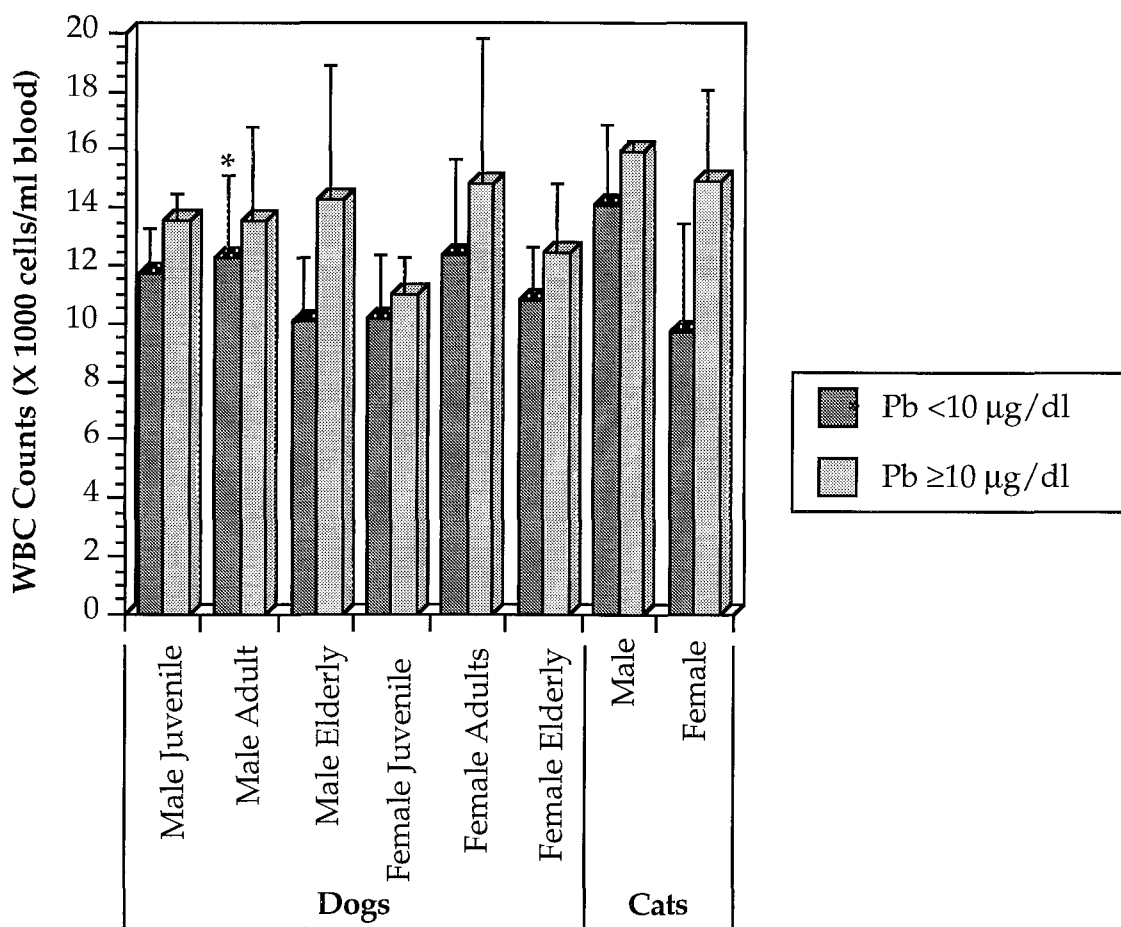
* significant difference p ≤ 0 10

3.6 Basophilic Stippling

Blood smears were examined for RBC, basophilic stippling and other morphologic abnormalities No basophilic stippling was observed Nucleated red blood cells were seen on 6 slides only, all in dogs with BLC above 12 µg/dl.

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3.7 Soil, Dust, Paint and Water Lead Concentrations

Soil lead concentrations ranged from < 100 ppm to 4,400 ppm (median 388 ppm, 75th percentile· 750 ppm) Dust lead concentrations ranged between 110 and 25000 ppm (median. 540 ppm, 75th percentile· 940 ppm) Figure 9 presents the range of concentrations, for dust lead versus soil lead concentrations in actual values, using logarithmic scales, but regressions were computed using log of concentrations

Figure 9: Relationship between dust lead and soil lead concentrations
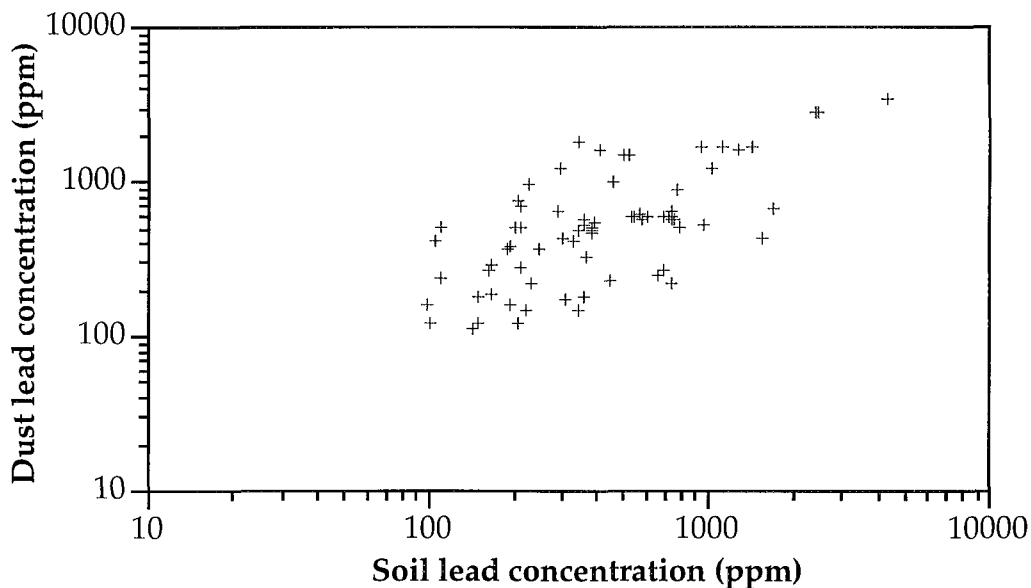
All water samples had lead concentrations below the level of detection of 5 μg/dl, and these values were not included in the report

Air lead levels higher than the USEPA standards were not reported since 1982 (Agency for Toxic Substances and Disease Registry, 1989). No air-specific measurements were performed in the dwellings

Paint lead levels in the subpopulation of people with pets were not found to be above 6 mg/cm2, except for 3 outliers When analyzing the association between soil, dust and BLC, these three (3) outliers were removed, because they skewed the distribution of residuals (Ott, 1988)

A stepwise multiple linear regression model was developed for BLC in pets. Among the numerous non-quantitative variables tested (Table 3), only one appeared significantly associated with higher BLC in dogs living on bare ground Therefore, we attempted to include it as a dummy variable in the final model When the model was computed, this variable no longer appeared significantly associated with log BLC in pets, and it had to be removed from the model No association was found between any other kind of soil cover, food, water source, bowl used to feed the animal, behavioral

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characteristics (chewing habits, pica, digging holes, restrained inside or running free), presence of a smoker at home and BLC in dogs or cats

Significant associations were found between BLC and species, soil lead concentrations, paint lead and average time (daily) spent outside by the animal

The final model yielded a coefficient of determination $r^2 = 0\ 37$ (p<0 001), i e 37 % of the variation in BLC in pets could be accounted for by the different variables included in the model The most important component in this model was soil lead concentration ($r^2 = 0\ 24$)

Odds ratios and Mantel-Haenszel adjusted odds ratios were computed for people and pets, to determine if living in a house with soil/dust lead concentrations above 500 ppm or 1,000 ppm increased the likelihood of having a high BLC Results are presented in Tables 9-12 Basically, the risk was not significantly increased for humans, while it was significantly increased for pets

Regression analysis was conducted to compare BLC in pets and people living in the same household Initial analysis of the data showed (Table 2) that there was a strong correlation between male and female among each age group in humans Therefore, data were analyzed based on age only in humans Table 13 summarizes the slopes, simple regression coefficients and coefficients of deter-mination, as well as p values and sample size for all the subgroups studied Because of the limited number of adults included in this part of the study, it was not possible to compute weighted correlation coefficients with pets living outside or inside, therefore all animal data were used together

Significant associations were found between BLC in younger children, school-aged children, and BLC in outdoor or indoor pets The most significant association was found between indoor animals and younger children (≤ 6 years old), and the second most significant association was found between school-age children and indoor pets The association between adults' BLC and pets was not significant

Table 14 is used to estimate the likelihood that any member of the family will has a high BLC, knowing that one pet has a high BLC Odds ratio were used to estimate the relative risk, because this was a prevalence study The odds ratio was 5 44, with a confidence interval (p<0 05) 1 47-21 04

The Yates' corrected Chi square test showed that the significance level was 0 006 Therefore, the likelihood of finding at least one person with a high BLC in a house where one pet at least had a high BLC was significantly increased

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Table 10: Odds ratios (OR) for high blood lead concentrations (BLC) ($\geq$ 10 µg/dl) for three groups of people, based on age, exposed to soil lead concentrations above 500 or 1,000 ppm

	Soil lead threshold concentration	
	500 ppm	1,000 ppm
< 7 years old (a, b, c, d)[1]	8, 31, 8, 58	6, 13, 10, 76
7-14 years old (a, b, c, d)[1]	1, 20, 1, 24	1, 10, 1, 34
> 14 years old (a, b, c, d)[1]	0, 14, 1, 14	0, 5, 1, 23
OR* of high BLC when soil lead > threshold	1 3	2.8
MHOR**	1 5	3 1
95% Confidence interval for MHOR***	0 5-4 5	0 9-9 8
OR <7 years old	1 90	3 50
OR 7-14 years old	1 20	3 50
OR > 14 years old	0 00	0 00

1 a, b, c, d   sample size for contingency tables   a BLC$\geq$10, soil>threshold, b BLC < 10, soil > threshold; c· BLC $\geq$ 10, soil < threshold, d. BLC < 10, soil < threshold

* OR the odds that a "case" is exposed divided by the odds that a "noncase" is exposed

**MHOR· OR adjusted for a potential confounder (age in this example)

***Exact limits (Mehta C.R., Patel N R , Gray R *J Am. Stat. Assoc* 80· 969-973, 1985)

Table 11: Odds ratios for high blood lead concentration (BLC) (≥ 10 μg/dl) for three groups of people, based on age, exposed to dust lead concentrations above 500 or 1,000 ppm

	Dust lead threshold concentration	
	500 ppm	1,000 ppm
< 7 years old (a, b, c, d)[1]	9, 49, 7, 40	5, 21, 11, 68
7-14 years old (a, b, c, d)[1]	1, 28, 1, 16	1, 14, 1, 30
> 14 years old (a, b, c, d)[1]	0, 18, 1, 10	0, 7, 1, 21
OR* of high BLC when dust lead > threshold	0 8	1 3
MHOR**	0 8	1.4
95% Confidence interval for MHOR***	0 3-2 5	0 4-4 4
OR <7 years old	1.0	1 5
OR 7-14 years old	0 6	2 1
OR > 14 years old	0 0	0 0

[1] a, b, c, d   sample size for contingency tables   a BLC≥10, dust >threshold, b. BLC < 10, dust > threshold, c BLC ≥ 10, dust < threshold, d. BLC < 10, dust < threshold

* OR   the odds that a "case" is exposed divided by the odds that a "noncase" is exposed

**MHOR   OR adjusted for a potential confounder (age in this example)

***Exact limits (Mehta C.R., Patel N R , Gray R   *J Am Stat Assoc* 80· 969-973, 1985)

Table 12: Odds ratios of high blood lead concentrations ($\geq$ 10 μg/dl) for pets living outside versus inside, exposed to soil lead concentrations above 500 or 1,000 ppm

	Soil lead threshold concentration	
	500 ppm	1,000 ppm
Pets outside (a, b, c, d)[1]	15, 9, 8, 18	9, 1, 14, 26
Pets inside (a, b, c, d)[1]	6, 14, 1, 35	3, 2, 3, 48
OR* of high BLC when soil lead > threshold	5 4	17 4
MHOR**	5 4	18 7
95% Confidence interval for MHOR***	1 8-16 8	3 6-138 1
OR pets outside	5 0	16 7
OR pets inside	15 0	24 0

[1] a, b, c, d   sample size for contingency tables   a BLC$\geq$10, soil>threshold, b BLC < 10, soil > threshold, c BLC $\geq$ 10, soil < threshold, d   BLC < 10, soil < threshold

* OR   the odds that a "case" is exposed divided by the odds that a "noncase" is exposed

**MHOR. OR adjusted for a potential confounder (pet living outside versus inside)

***Exact limits (Mehta C R , Patel N R , Gray R   *J. Am. Stat. Assoc* 80   969-973, 1985)

Table 13: Odds ratios of high blood lead concentrations (≥ 10 μg/dl) for pets living outside versus inside, exposed to dust lead concentrations above 500 or 1,000 ppm

	Dust lead threshold concentration	
	500 ppm	1000 ppm
Pets outside (a, b, c, d)	21, 12, 2, 15	12, 1, 11, 26
Pets inside (a, b, c, d)	6, 20, 1, 29	4, 5, 2, 45
OR* of high BLC when dust lead > threshold	12 4	14.6
MHOR**	11 2	23.7
95% Confidence interval for MHOR***	2 8-63 6	4.8-128.9
OR pets outside	13 1	28.4
OR pets inside	8 7	18.0

[1] a, b, c, d   sample size for contingency tables   a: BLC≥10, dust>threshold; b BLC < 10, dust > threshold, c BLC ≥ 10, dust < threshold, d   BLC < 10, dust < threshold

**OR   the odds that a "case" is exposed divided by the odds that a "noncase" is exposed

**MHOR· OR adjusted for a potential confounder (pet living outside versus inside)

***Exact limits (Mehta C R , Patel N R., Gray R. *J Am. Stat. Assoc* 80   969-973, 1985)

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Table 14: Correlation between blood lead concentrations of pets and people living in the same household

Pets	Humans (years)	N	r	ß	SD (ß)	p-value
Pets Outside	Child ≤ 6	64	0 61	0 09	0 02	<0 001
	Child 6-14	30	0 43	0 1	0.03	<0 001
Pets Inside	Child ≤ 6	49	0 93	0 35	0 02	<0 001
	Child 6-14	26	0 74	0 26	0 03	<0.001
All Pets	Adults	29	0 22	0 08	0 14	0 6

r = correlation coefficient

β = Slope of the regression line

SD (ß) = standard deviation around ß

Table 15: 2x2 table and odds ratio (OR) for cases and noncases in animals and humans within one household

		Humans		
		Case	Non Case	Total
Pets	Case	10	15	**25**
	Noncase	6	49	**55**
	Total	**16**	**64**	**80**

OR = 5 44 - 95% Confidence Interval = (1 47-21 04)

$\chi 2$ = 7 36 (Yates' Correction) p=0 006

Cases households where at least one person or one pet had a high BLC ($\geq 10\mu g/dl$)

Noncases households where no pet or no person had a high BLC

Prevalence = 16/80 = 20%

Sensitivity = 10/16 = 62 5%

Specificity = 49/64 = 76 6%

Predictive Value of a Positive Test = 10/25 = 40%

Predictive Value of a Negative Test = 89 1%

Chapter 4. Discussion

4.1 Blood Lead Concentrations in Humans and Pets

As mentioned earlier, a cut-off value of 10μg/dl BLC was used, based on the latest recommendations of the CDC in humans, to define a "case" Because of the similar response of dogs and humans, it was reasonable to use this value in dogs as well (Scharding and Oehme, 1973) For consistency of data, it was decided to use the same value in cats, but lead toxicity has been much less studied in that species and there is a definite lack of information for cats The first conclusion that could be drawn from the different proportions of animals and humans with BLC ≥ 10μg/dl was that household pets tended to be more at risk of having an increased BLC than people when exposed to a similar environmental lead source Species-related behavioral patterns could probably explain most of the differences dogs chew on objects, lay in the dirt and dig holes Cats groom themselves very carefully when exposed to excess dirt or dust, which exposes them to tiny particles of lead from contaminated soil or paint chips, as has been reported in other studies (Jacobs, 1981, Watson, 1983, Morgan et al, 1991) It should also be mentioned that window sills were often found to contain higher concentrations of lead than any other areas in a dwelling (Schwartz and Levin, 1991) Because cats often sit near windows, they are exposed to the higher concentrations of lead In our study, the difference between cats and humans was not significant. It has been shown repeatedly that young children could be at risk of excessive lead intake from soil contamination because of their hand-to-mouth activity (especially children less than 3 years of age) In this particular study, infants did not appear to be overly exposed to lead from soil, since the proportion of high BLC among them was low Besides, in most instances, it was found that children with high BLC were either exposed to lead-based paints, or exposed to lead via their parents' activities (occupational exposure, preparing lead bullets e g) A follow-up study done on those children found that BLC were much lower when these other lead sources were removed or properly managed (Kimbrough et al, 1992) In our subpopulation of people with pets, environmental data did not suggest any severe exposure from lead-based paints An interesting feature was that the proportion of people with a BLC ≥ 10μg/dl was not significantly different between people with and people without pets However, mean log BLC were different (p ≤ 0 05) Some authors (Thomas et al, 1976) have hypothesized that young children may imitate the behavior of animals and have increased chewing activity when there is a dog around Another suggested explanation was that dogs coming in and out may bring in more lead-contaminated dust from outside, and often questions regarding animals movements are included in questionnaires (CDC, 1989) Our data would rather suggest that there was a very limited increased risk of lead exposure for younger children associated with the presence and movements of pets in a house.

Among people with one household pet, several important features were noted Correlation analysis showed that sex was not a confounder, whereas age appeared to be a major confounder the only highly significant correlations could be found between males and females within each age group (Table 2) Many studies have shown that both

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variables can affect the BLC distribution Most of the time, different behavioral patterns between boys and girls explain this sex-related difference Also, young children are more at risk of increased lead-exposure, because of their hand-to-mouth activity, and they had higher BLC than older people in this study. Mean BLC (log transformed data) was low compared to prior studies (Abbriti et al, 1988; Amler et al, 1988, CDC, 1989, Green et al, 1976) The proportion of people with BLC $\geq$ 10 µg/dl was also low. One reason for that could be that air-borne lead, which used to be considered a major source of lead, was not significant in that particular situation, since leaded gasoline was not used much any more (Ducoffre et al, 1990) Also, as mentioned in some other lead studies, because of the dramatic lowering trend observed in BLC over the past 15 years, results from studies conducted more than one year apart, even in very similar environments, will generally be very different (Amler et al, 1988) Another explanation could be that local soil characteristics decreased the availability of lead Several studies in plants have shown that the soil cation exchange capacity and pH can dramatically affect the availability of lead (Hasset and Miller, 1977, Zimdhal and Koeppe, 1977) In wild rodents, it was suggested that pH and calcium content of the soil could affect the amount of lead found in bones and soft tissues However, the published results were not statistically significant, probably due to the limited number of animals trapped (Roberts and Honson, 1978) As discussed by Schwartz and Levin (1991), studies around lead smelters have also often yielded lower results, as far as BLC, than expected, based on more general soil lead blood lead relationship studies Hypothesized reasons for this conclusion is the larger particle size of lead deposits, the chemical nature of lead (which influences its bio-availability) and the possible increased awareness of people living around a smelter

Some studies have been reported in which dogs or cats were used to assess lead exposure to humans (Watson, 1983, Thomas et al, 1976, Koh and Babidge, 1986) They all concluded that finding a high BLC in a house dog increased the likelihood of finding one person with a high BLC Thomas et al (1976) estimated that the likelihood was 6-fold greater, which is almost identical to our result Zook (1978) considered dogs and children to be very similar in their susceptibility to lead and risk of exposure from environmental sources According to him, young dogs would even develop clinical signs of lead poisoning before young children did, therefore emphasizing the potential use of household dogs as sentinels of excessive lead exposure to children In some countries, like Australia and New Zealand, it is mandatory for veterinarians to report lead poisoning cases to human health authorities (Watson, 1983) Koh (1987) considers that physicians and veterinarians should work closer to better address the issue of lead poisoning in children Our results showed that dogs and cats could be used interestingly to monitor lead exposure It is interesting to mention that the stronger associations were found between younger children and pets, which confirmed Zook's finding, that dogs reflect what can be found in young children (Zook, 1978) Our result suggest that animals were at a higher risk of having high BLC than children, considering they were exposed to similar sources (i e soil, dust and paint) Interestingly, the most significant association was found between inside-dogs and younger children. This is in agreement with the prior finding that dogs and children sharing the same environment were both at higher risk of increased lead exposure than

other people in the same dwelling (Zook, 1978) Correlation analyses showed that there was a similar trend in human and animal BLC The odds ratio analysis showed that when a dog or a cat was found to have a high BLC, the likelihood of finding one person in that household with a high BLC was significantly increased. Our data show that the negative predicitive value is 89 1% (Table 14) This means that if no animal in the household is found with a BLC ≥ 10 µg/dl, no human will have a BLC ≥ 10 µg/dl in about 90% of the cases This is explained by the fairly high specificity of the test and also by the low prevalence (20%) of BLC ≥ 10 µg/dl in people Should the prevalence be 80%, then the positive predictive value would be more reliable Therefore, testing dogs or cats could be a very simple tool to measure the risk of excessive soil lead exposure for the entire family Our results confirmed findings reported by Thomas et al (1976), who, however, did not describe the sources of lead involved

4.2 ALAD Activity in Dogs and Cats

ALAD activity has been consistently reported to be inhibited by lead in humans (Nikkanen et al, 1972, Paglinca et al, 1990) dogs (Berny et al, 1992a), cats (Berny et al, 1992a), cattle (Bratton, 1986), sheep (Rolton et al, 1978), and birds (Scheuhammer, 1987) It is a common and inexpensive test used to assess exposure to lead, rather than lead toxicosis It is considered a very sensitive and specific criterion for lead exposure, responding to BLC around 10 µg/dl (Moore et al, 1980; Bortoli et al, 1986) However, falsely decreased activities can be observed with elevated alcohol consumption or severe anemias (Bortoli et al, 1986) The former is not likely to be a problem with a pet population; the latter can be ruled out by measuring PCV, hemoglobin concentrations, and red blood cell counts None of these parameters indicated that dogs or cats in the present study suffered from anemia There was a negative linear relationship between BLC and log ALAD activity In our study, the relationship was strong, even at low BLC Since no information on ALAD activity is available in cats, results are presented separately for each species In a preliminary study (Berny et al, 1992a), ALAD activity was inhibited *in vitro* very similarly in both species, but no information was available on the *in vivo* effects of lead on ALAD

A wide range of values for ALAD activity was observed (78 to 1000 nMol Porphobilinogen/ml RBC/hour) Different subgroups were analyzed separately because prior studies in other species showed that age could influence the ALAD activity as well as the relationship between that activity and BLC (Bratton et al, 1986) In young dogs and cats together, linear regression analysis yielded a correlation coefficient of -0 95 (-0 93 for dogs by themselves, not significantly different p<0 05) This was very high for a field experiment and was close to results reported in the literature for various species, including humans In older dogs and cats, the correlation coefficient was lower -0 74 (in dogs only, r=-0 76, not significantly different p<0 05), but the number of animals tested was very small (only 6) In adult dogs, the relationship was stronger with r=-0 86 One outlier decreased the correlation, and analysis without this outlier yielded a linear regression coefficient r=-0 92 No explanation was found for that outlier The relationship in adult cats was very close to that observed in adult dogs, and both groups could be studied together, since there was no significant difference

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between regression lines The relationship between BLC and ALAD is considered strong for BLC above 10 μg/dl (Bortoli et al, 1986) In our study, the relationship, as measured by the corrrelation coefficient, remained high, even though many BLC values were between 5 and 10 μg/dl. Therefore, it appears that ALAD activity remains the most sensitive test for lead exposure, and it also seems that dogs and cats respond in a very similar fashion to lead. The limitations for ALAD activity are that this test must be performed on fresh blood and that there is a wide range of variation for normal values, therefore, it can only be used to study a population and it will not be as useful to assess the lead-exposure status in a single animal

4.3 FEP Concentration in Dogs and Cats

FEP is often measured in humans, as zinc protoporphyrin (ZPP), with an hematofluorometer It is an inexpensive and easy test and the concentration of FEP in blood is related to the turn-over rate of RBC (Needleman et al, 1990) Therefore, it reflects an exposure that has been occurring over three months It is not often measured in animals. Koh (1985) reported use of this test on a regular basis, as well as BLC, to determine whether lead exposure was chronic or acute Milhaud et al (1990) reported that ZPP is not a reliable and sensitive test in lead-poisoned dogs It may well be that dogs, like cattle, (George and Duncan, 1980) respond to lead by increasing protoporphyrin IX without always incorporating zinc into it, and, therefore, not increasing ZPP as much. In this study FEP was measured, which accounts for all the protoporphyrins, since the acid extraction removes the zinc ion Other porphyrins do not increase significantly and usually account for less than 5% of total FEP (George and Duncan, 1980). Our study suggested that FEP can be used to determine the extent of chronic lead exposure in dogs and cats Yet, the effects were observed only at BLC $\geq$ 20 μg/dl, which was very similar to what was noticed in humans (Needleman et al, 1990). In several human studies, a 10 fold increase of ZPP was reported after lead exposure In this field study, FEP values were only 3 times higher in dogs with higher BLC. However, since data above 20 μg/dl blood lead were limited, it should not be concluded that the response in dogs was not as important as it is in humans. Further laboratory or field studies are needed to determine precisely the limits of the FEP test in dogs At lower lead levels (< 20 μg/dl), FEP did not seem sensitive, as observed in humans (Needleman et al, 1990) A recent study (Hawke et al, 1992) reported normal FEP values as well as elevated values associated with lead poisoning in cats The values found for cats in our study were similar to those found "normal" by those scientists the mean FEP concentration in cats was 223 ($\pm$ 186) μg/l, while our study gave a mean value of 446 ($\pm$ 219) μg/l, which was not different (p<0 05) The authors also determined that ZPP would be as reliable, since it accounted for most of the increase in total protoporphyrin (no precise % given). The FEP concentrations reported in lead-poisoned cats were somewhat higher. There was also an important overlap between "normal" levels of FEP and levels found in lead-poisoned cats. Since FEP was measured in only 3 cats with clinical lead poisoning, it seems that some more studies should be conducted to evaluate the use of FEP to signal chronic lead poisoning in cats Among the few animals with a BLC > 20μg/dl, the increase in FEP was important enough and there did not seem to be any overlap between pets with a BLC > 20 μg/dl

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and pets with a lower BLC, as far as FEP concentrations. However, it would be interesting to validate this finding with more dogs and cats

4.4 Serum Chemistry Profile

It has been shown previously that prolonged lead exposure can cause chronic interstitial nephritis in humans and, to a lesser extent, in animals (Bernard and Becker, 1988; White, 1977) It is common practice to check animals for BUN and creatinine serum concentrations to monitor their renal function (Fraser et al, 1991). In clinical cases of lead poisoning, elevated creatinine concentrations have been reported (Morgan et al, 1991, Paglinca et al, 1990) In this study, no difference was observed between "cases" and "non cases", either because BUN and creatinine were not sensitive enough or because BLC were too low to adversely affect the kidneys Indeed, many authors consider that renal function is not altered in humans or animals until high BLC are reached (80 µg/dl) (Bernard and Becker, 1988, Morgan et al, 1991) Statistical analysis of our data showed that even in older dogs there was no significant difference between cases and non cases, with respect to BUN and creatinine concentrations No clinical test that can be easily performed and that would be an early indicator of renal changes in humans has been found to signal lead-induced renal disorders (Bernard and Becker, 1988) The conclusion from this study is that the possiblity of an effect of lead on the kidney at low blood lead concentrations in animals could not be ruled out, but that the routine tests used here were not sensitive enough to detect minor changes.

AST, ALT and alkaline phosphatases are very often used in veterinary practice to investigate hepatic function (Fraser et al, 1991). All the data given here were within normal ranges (except for one outlier), but significant differences were observed between cases and non cases, concerning ALT and AST in dogs The pattern of response for each age-sex group was also significantly different in dogs (i e. the response was different for each of these groups) In lead poisoning, elevated values for the serum liver enzymes have been inconsistently observed in humans and animals (Paglinca et al, 1990). They also seem to appear at high BLC (> 40 µg/dl) Because variations are limited and not consistent between groups, these results may be spurious and do not appear to be biologically significant.

Significant differences between cases and non cases, within each species were seldom observed. Because of the number of tests performed, some of those differences were probably related to random variation and additional studies are needed to assess those effects Whenever a significant difference was noticed, we investigated it more thoroughly and tried to adjust for species, sex and age No test was found to give consistent results, therefore these may be spurious results Other studies reported alterations in cholesterol and glucose concentrations (Hamir, 1986, Milhaud et al, 1990) It is possible that these effects, which are not considered specific (Zook, 1978), may also be insensitive indicators, and only yield significant results in clinical cases of lead poisoning. It is a common finding, for instance, to notice altered blood glucose after episodes of tremors or seizures, which are often seen in lead-induced encephalopathy (Milhaud et al, 1990)

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4.5 Complete Blood Cell Counts

In humans, chronic lead exposure may eventually cause some decrease in hemoglobin synthesis, as measured by hemoglobin concentration (Moore et al, 1980, Poulos et al, 1986) Lead is also believed to alter hemoglobin concentration at very low BLC, around 10 μg/dl (Mushak et al, 1986; Poulos et al, 1986) In animals, this effect is not as prevalent, although it has been reported in dogs (Canfield et al, 1986; Bernard and Becker, 1988) and cats (Jacobs, 1981) Hemoglobin concentrations were significantly different between cases and non cases in adult dogs but not in any other group, possibly because of the smaller sample size Hemoglobin in dogs is often considered to be less susceptible to lead (Osweiler et al, 1985). However, this might reflect a lack of data for dogs in the lower range of BLC This is the first time that such low blood lead concentrations were associated with lowered hemoglobin concentrations in dogs It has been reported in humans that 10 μg/dl BLC is a threshold for lead-induced anemia (Poulos et al, 1985) The hemoglobin levels reported in our study remained in normal ranges, therefore, hemoglobin concentrations might not be appropriate to assess lead exposure in dogs Likewise, changes in neither PCV, nor RBC counts were associated with increased BLC Therefore, these parameters might not be useful to signal lead-induced anemia in dogs or cats

Very few data are available on the effects of lead on white blood cells in dogs or cats. Increased WBC counts were reported with lead poisoning, but no threshold was determined (Morgan et al, 1991) In our study, WBC counts were increased in both dogs and cats with BLC ≥ 10 μg/dl; however, values were still within the normal ranges for both species Reasons for such alterations are not understood, and only limited attention has been given to WBC changes in lead poisoning. Milhaud et al (1990) reported increased WBC counts in dogs with clinical lead poisoning and attributed it to a non specific stress reaction.

4.6 Basophilic Stippling

Basophilic stippling without anemia has frequently been reported as the most common change in RBC in lead poisoning in dogs (Zook, 1978, Berny et al, 1992b) It appears soon after lead exposure (less than a week), at higher BLC (35 to 50 μg/dl) than those encountered in our study No positive slide could be found in our study, probably because of the low BLC found. In some instances (Morgan et al, 1991), nucleated RBC were associated with lead poisoning This is an indirect effect of lead because of increased fragility of RBC, and reduced life span of RBC, some degree of regenerative anemia can be expected in animals exposed to lead and, therefore, more nucleated red blood cells may be in circulation Nucleated red blood cell count is not a specific test to signal lead exposure and it is not very sensitive either, since positive slides were found only in a very small proportion of the dogs with higher BLC In an analysis of data reported to animal poison control centers, RBC changes occurred in less than 10% of the clinically affected dogs and cats (Berny et al, 1992b).

4.7 Soil, Dust, Paint and Water Lead Concentrations

In this study, we attempted to determine whether 500 ppm or 1,000 ppm lead in soil or dust could be considered a significant hazard to human or pet health, and whether dogs and/or cats would be suitable sentinels of human exposure. Our results suggest that household pets were more likely to have a high BLC than were their owners The limited number of humans (198) and animals (107) included in our study must be kept in mind We also determined the best linear fit between soil lead and BLC (after log transformation), adjusted for age in humans Of the potential covariates that were tested, age was the only one found to be significantly associated with BLC changes in humans, and was therefore included as a con-founding factor in the determination of odds ratios Because young children may ingest more soil and dust than older children and adults, age is very important to estimate the likelihood of exposure via soil or dust ingestion (O'Heany et al, 1988; Schilling and Bain, 1988) Several studies have been reported that attempted to link environmental lead contamination with BLC in humans (Amler et al, 1988, O'Heany et al, 1988, Schilling and Bain, 1988, Madhavan et al, 1989, Maravelias et al, 1989, Center for Disease Control, 1987) Significant associations between soil lead and BLC have been reported and summarized by Steele et al (1990), with ß ranging from 1 1 to 7 6, i e there was an increase in BLC in children from 1 1 to 7 6 µg/dl blood per 1,000 ppm increase in soil lead, with soil lead concentrations up to 5,000 ppm Compared to slopes measured in mining towns or in general urban areas, those determined in places where a lead smelter was in operation are usually small (Steele et al, 1990) In our study, coefficients of correlation, although significant, were small, indicating a weak relationship. Slopes of the regression lines were very flat and would correspond to an increase of 1.4 µg/dl lead in blood when soil lead increases from 1 to 1,000 ppm Because of the double logarithmic transformation, the increase in BLC would be even lower with an increase in soil lead from 1,000 to 2,000 ppm (1 1 only) Therefore, our results were consistent with the published ranges of slopes, even though they were in the lower part of that range This could be partially explained by the low BLC range reported, compared to other studies Schilling and Bain (1988), for instance, reported higher correlation coefficients, and steeper slopes than those calculated here The range for soil lead concentration was larger (53-21,000 ppm in soil, 80-19,000 in dust) They also had a wider range for BLC in children (1-45, compared to 1-13 in this subgroup) Because of the small BLC range, we did not attempt to adjust the low corre-lation coefficients and significance levels for other covariates However, odds ratios were never found to be significant in humans Even when the soil was contaminated with lead above 1,000 ppm, the probability of having a BLC $\geq$ 10µg/dl was not significantly increased for any age group of people (Tables 2 and 3)

The increase in BLC associated with soil contamination by lead, as shown by the linear regression and the odds ratios, was very low and would not support the current value of 500 or even 1,000 ppm as the threshold for remedial action (Center for Disease Control, 1985) However, to interpret this result it must be kept in mind that BLC is only a measure of recent lead exposure and does not correlate with the total body burden of lead Bone lead, which is a good indicator of the total amount of lead in the

body, may be a more reliable indicator of potential detrimental effects (Wielopolski et al, 1986, Schütz et al, 1987, Silbergeld, 1990)   Also, measurement of soil and dust lead concentrations does not always give information about availability of lead. A complete evaluation should also include the determination of the chemical nature of lead in the contaminated site, particle size and soil characteristics, such as cation exchange capacity and pH   Even in one contaminated site, those factors may vary considerably Therefore, it seems advisable to determine suitable monitors of the bio-availability of lead in soil

In pets, a significant association between soil lead, dust lead and BLC was found The relationships between environmental lead and pet BLC were much stronger than those found for animal owners   Similarly, odds ratios were significant for both 500 and 1,000 ppm soil and dust threshold levels, with larger values in the latter case   These results suggest that dogs and cats were more at risk of having a high BLC than were humans in a similar environment   Findings consistent with ours were reported with dogs only (Thomas et al, 1976) and the idea of using household pets as monitors of lead exposure has been proposed elsewhere (National Research Council (1991)   The study of Thomas et al (1976) focused on dogs and children within one household, and they concluded that finding an increased BLC in a dog increased the likelihood of finding an increased BLC in a child by 6 fold. Two limitations of their study were that the lead source was not described, and also that BLC were much higher. a "high BLC" was defined as 35 μg/dl in dogs and 40 μg/dl in children, which is higher than current accepted standards (CDC, 1985)   It should be remembered that in the present study a concentration of 10 μg/dl was used to define a "case" (high blood lead) in the animal population, as used in humans, based on the CDC recommendations   The range of BLC was <5 to 28 μg/dl, which is below concentrations at which clinical signs may occur in dogs (35 μg/dl, Zook, 1973). No adverse health effects in any animal were found However, changes in biological markers associated with BLC $\geq$ 10 μg/dl were found (higher white blood cell counts, lower hemoglobin concentrations), but the values were within normal ranges, and the biological significance of such modifications is questionable   We also measured ∂ amino-levulinic acid dehydratase (ALAD) inhibition and found that there was a linear relationship between log ALAD and the log BLC (see Table 5)   Erythrocyte protoporphyrin, which is also used as an indicator of chronic lead exposure, was not significantly elevated, except for those animals with a BLC$\geq$20 μg/dl, a lead concentration also reported as the threshold value in humans and cattle for increased FEP (Pinault and Milhaud, 1983; Parsons et al, 1991)   Therefore, very few significant adverse effects could be associated with these low BLC.

Multiple linear regression showed that there was colinearity between lead concentrations in soil, dust and paint   Rabinowitz and Bellinger (1988) reported a similar finding, when trying to estimate the slope of the best linear fit between soil or dust lead and BLC in children   These authors calculated slopes and correlation coefficient between BLC and either soil or dust lead, with or without adjustment for this collinearity   Correlation coefficients ranged from 0 15 to 0 30, which was very similar to results in this study, even though we did a log transformation of lead concentrations (environmental and blood)   In the present paper, including or not including paint lead

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in the model did not significantly improve the model, therefore, paint lead was not included as a variable Adjusted partial correlation coefficients were lower, when both variables were included in the model The overall correlation coefficient was 0 37, which is close to what was reported in a report by Arnetz and Nicolich (1990) (r^2 = 0.35), who used the National Health and Nutrition Examination Survey (NHANES II) data, and tried to develop a model for blood lead in humans Ducoffre et al (1990) found a somewhat higher r^2 (r^2 = 0 50) with airborne lead and several environmental and behavioral parameters in their model

Contrary to what was found in children in other studies (Center for Disease Control, 1987, Amler et al, 1988, O'Heany et al, 1988, Rabinowitz and Bellinger, 1988), none of the behavioral or environmental covariates assessed improved our model, i e. pica, chewing activity were not significantly associated with changes in BLC in pets Several authors have reported that a grass-covered soil reduced the availability of lead to children, as shown by lower BLC, probably because less particles were resuspended in the air (Steele et al, 1990) Our study does not substantiate this finding for pets there was no difference in BLC in pets spending most of their time either on a grass-covered soil, or on concrete, sand or bare ground soils. Passive smoking has also been shown to be associated with higher BLC in humans (Ducoffre et al, 1990) In the present study, there was a strong negative relationship between the time spent outside and the exposure to cigarette smoke by pets. However, after adjusting for the time spent outside, passive smoke was not significantly associated with higher BLC.

It appears, therefore, that household pets are more at risk of having high BLC than their owners are, when lead is present in soil and house dust. Despite the lack of information regarding the nature of lead in soil or particle size, it seems that pets were actually absorbing lead. Soil maps of the sampling site and discussion with an agronomist (Hasset J J University of Illinois, Department of Agronomy, personal commnication) showed that soil characteristics were most likely very similar throughout the area studied (Soil Conservation Service, 1986) The likelihood of finding a person with a BLC $\geq$ 10µg/dl was significantly increased when at least one household pet was found to have a BLC $\geq$ 10µg/dl (see Table) Taking blood samples from dogs and cats is an easy and non-invasive technique Our experience with the people in this study taught us that samping their pet was not considered to be as stressful an experience as taking a blood sample from a very young child was Sampling can be done on a routine basis to monitor pet BLC during an annual visit to a veterinarian for immunization and health maintenance purposes If BLC are higher than background (e g $\geq$ 10µg/dl), it would be advisable to have the pet's owners tested as well.

Chapter 5. Conclusions

Our first conclusion is that household pets were more at risk than their owners of having a high BLC when exposed to a similar environment

Our second conclusion is that, despite the increased risk from soil contamination, the overall BLC in humans and animals were very low and were generally below the recently established threshold of 10 µg/dl

Soil lead concentrations should not be used as the only parameter of choice to estimate the risk of increased lead absorption, since many other factors can affect the availability of lead to mammals (Steele et al, 1990) To establish a potential risk associated with a given lead-contaminated soil, the concentration should be considered cautiously in conjunction with soil characteristics, lead particle size and chemical form of lead, as well as behavioral features of both animals and humans

Our study did show that there was a relationship between soil lead concentrations and BLC in dogs Since the study area was small and located around a smelter, it was considered that most environmental and lead-associated variables were very similar across that area, and therefore did not influence the overall relationship between soil lead concentrations and BLC

Finally, establishing regulatory remedial action levels based only on lead concentrations in soil or dust does not appear to be legitimate On the other hand, attempting to include all the environmental variables would certainly be a long and expensive process Therefore, we consider that using dogs and cats as monitors would be the most efficient way to determine the risk to humans, if any, associated with a lead-contaminated environment

Recommendations

Based on our results, it appears that dogs and cats are more exposed than their owners to lead in soil or dust. There is a strong, positive relationship between BLC in animals and their owners, especially pre-school children. Because testing an entire population potentially exposed to lead is such a costly and stressfull process, it is our suggestion to test dogs and cats instead. If none of the animals tested in the household has a BLC $\geq$ 10 μg/dl, it is very unlikely that any of the residents will have a BLC above that limit, given that there is no occupational exposure of the adults. If there is one, or more, positive tests in the animals, it is recommended that humans in the household be tested as well

This procedure would certainly give reliable results and reduce the cost and stress level associated with the testing of young children. Dogs and cats behave as biological markers, integrating all the variables that influence the availability of lead to mammalian systems. Thus, they would provide more reliable information about the hazards associated with lead wastes than would environmental testing

References

Abbriti G., C. Cicioni, M. Gambelunghe, T Fiordi, M.P. Accattoli, P Morucci, E Bellucci, F A Bauleo 1988 Blood lead levels in children living in three communities, at different risks of lead pollution *Biomed. Env. Sciences*, 1 363-371

Agency for Toxic Substances and Disease Registry 1989 *Preliminary health assessment for NL Industries/Taracorp lead site Granite city, Madison county, Illinois* Atlanta ATSDR, US Dept Public Health

Amler R D , S B Baburich, P A. Jones, W E Kaye, J A Lybarger, B S Richter. 1988 *The Silver Creek mine tailings exposure study, Park City, Utah-Final Report* Atlanta· ATSDR, US Dept Public Health

Arnetz B.B., M.J. Nicolich. 1990 Modelling of environmental contributors to blood lead in humans *Int Arch Occup. Environ. Health*, 62 397-402

Berlin A , K H Schaller 1974 European standardized method for the determination of ∂-Aminolevulinic acid dehydratase activity in blood *Z Klin. Chem Klin. Biochem* , 12 389-390

Bernard B P , C E Becker 1988 Environmental lead exposure and the kidney *Clin Tox.*, 26 (1-2) 1-34

Berny P J., L M Côté, W B Buck 1992 Erythrocyte ∂-aminolevulinic acid dehydratase (ALAD) activity as an indicator of lead exposure in dogs and cats optimal test conditions *Tox. Met.*, 2 (1) 57-68

Berny P J , L M Côté, W B Buck 1992 Case reports of lead poisoning in dogs from the National Animal Poison Control Center and the Centre National d'Informations Toxicologiques Vétérinaires anecdotes or reality? *Vet human Toxicol .*, 34 (1) 26-31

Bloom H , B N. Noller, G Shenmann 1976 A survey of blood lead levels in dogs and cats *Aust Vet J* , 52 312-316

Bortoli A., G Fazzin, V Marin, G Trabuio, S. Zotti 1986 Relationship between blood lead concentration and aminolevulinic acid dehydratase in alcoholics and workers exposed to lead *Arch Environ. Contam Toxicol.*, 41 (4) 251-260

Bratton G.R , M Childress, J Zmudzki, C Womac, L D Rowe, Tiffany-Castiglioni 1986 Delta-aminolevulinic acid dehydratase (EC4 3 1 24) activity in erythrocytes from cattle administered low concentrations of lead acetate *Am J. of Vet. Res.*, 47 (9) 2068-2074

Buck W B 1979 Animals as monitors of environmental quality *Vet. human Toxicol* , 21 277-284

Canfield P J , A J Fairburn, A D J Watson 1984 Blood lead, urinary delta
aminolevulinic acid and the diagnosis of lead poisoning in dogs. *Aust. Vet.* J., 61
(10) 323-324

Cattaneo P , C Balzaretti 1987 Piombo in tessuti duri di cane e in denti umani *Arch.
Vet Italiano,* 38 (5/6) 88-95

Centers for Disease Control 1985. *Preventing lead poisoning in young children.* Atlanta
US Dept Public Health

Center for Disease Control 1987 *Leadville metals exposure study, Leadville, CO, Final
report* Atlanta US Dept Public Health

Center for Disease Control 1989 Surveillance for occupational lead exposure-United
States, 1987. J A M A , 262 (17) 2370-2372

Ducoffre G ,F Claeys, P Bruaux 1990 Lowering time trend of blood lead levels in
Belgium since 1978 *Environ. Res.,* 51. 25-34

Fraser C. M , J A Bergeron, A Mays, S. E. Aiello, eds 1991. *The Merck Veterinary
Manual, 7th Edition,* Rahway. Merck and Co , Inc

George J W , J R Duncan 1980. Erythrocyte protoporphyrin in experimental chronic
lead poisoning in calves *Am. J. of Vet Res ,* 42 (9) 1630-1637

Green V A , G W Wise, N W Smull 1973 Lead survey of selected children in Kansas
City and some unusual cases *Clin Tox ,* 6 (1)· 29-37

Hamir A N 1986 Review of lead poisoning in dogs *Vet Bulletin,* 56 (12) 1059-1070

Hamir A N , P D. Handson, N D Sullivan, G Anderson 1986. Lead tissue levels of
dogs from rural and urban areas of Victoria, Australia *Vet Rec ,* 118 77-78

Hasset J J , J E Miller 1977 Uptake of lead by corn from roadside soil samples
Commun in Soil Science and Plant Analysis , 8 (1)· 49-55

Hawke C G , J E Maddison, V Poulos, A D J Watson, 1992 Erythrocyte
protoporphyrin concentrations in clinically normal cats and cats with lead
toxicity *Res Vet Science,* 53: 260-263

Jacobs G 1981 Lead poisoning in a cat *J.A V M A ,* 179 (12) 1396-1397

Kimbrough R , M Levois, T Long, D. Webb. 1992 Lead study around a defunct
smelter *Vet human Toxicol ,* 34 (4) 360

Koh T S 1985 Diagnosis of lead poisoning in dogs *Aust Vet J ,* 62 (11) 392-394

Koh T S 1987 Lead poisoning closer liaison between medical and veterinary investigators *Med J Aust* , 146· 280

Koh T.S , P J Babidge 1986 A comparison of blood lead levels in dogs from a lead-mining, lead-smelting, urban and rural island environment. *Aust. Vet. J* , 63 (9) 282-285

Kucera E 1988 Dogs as indicators of urban lead distribution *Env. Mon Assess* , 10 (1) 51-57

Laxen D P , G M. Raab, M. Fulton 1987 Children's blood lead and exposure to lead in household dust and water A basis for an environmental standard for lead in dust *Sci Tot Env* , 66 235-244

Madhavan S , K D Rosenman, T Shemata 1989 Lead in soil recommended maximum permissible levels *Environ Res* , 49· 136-142

Maravelias C., A Hatzakis, K Katsouyanni, D Trichopoulos, A Koutselinis 1989 Exposure to lead and cadmium of children living near a smelter at Lavrion, Greece *Sci. Tot. Env* , 84 61-70

Matte T D , J.P. Figueroa, S Ostrowski, G Burr, L. Jackson-Hunt, R Keenlyside 1989 Lead poisoning among household members exposed to lead-acid battery repair shops in Kingston, Jamaica *Int J Epidemiol* , 18 (4) 874-881

Milhaud G , J P Boidot, B Joseph-Enriquez, E Charles, D. Balde . 1990 Intoxication par le plomb dans un chenil *Rec Med Vet* , 166 (10) 881-885

Moore M R., P.A Meredith, A Goldberg 1980 Lead and heme biosynthesis in *Lead toxicity* edited by Singhal R L , Thomas J A. 79-117 Baltimore Urban and Schwarzenberg

Morgan R.V , L K Pearce, F M Moore, T Rossi. 1991(a) Demographic data and treatment of small companion animals with lead poisoning 347 cases (1977-1986) *J A V M A* , 199 (1) 98-102

Morgan R V , F.M Moore, L K Pearce, T Rossi 1991 (b) Clinical and laboratory findings in small animals with lead poisoning 347 cases (1977-1986). *J.A V M.A.*, 199 (1). 93-97

Mushak P , J.M. Davis, A F Crocetti, L D Grant 1989 Prenatal and postnatal effects of low-level lead exposure integrated summary of a report to the U S Congress on childhood lead poisoning (review) *Environ Res* , 50 11-36

National Research Council 1991 *Animals as sentinels of environmental health hazards*, Washington, D C National Academy Press

Needleman H L., S E. Royce, et al eds (1990). *Case studies in environmental medicine. lead toxicity* Atlanta· ATSDR, US Dept Public Health

Nikkanen J , S Hernberg, S Tola 1972 Modifications of the ∂ aminolevulinic acid dehydratase test and their significance for assessing different intensities of lead exposure *Work, Environ , Health*, 9 46-52

O'Heany J , R Kusiak, C E Duncan, L F Smith, L Spielberg 1988 Blood lead and associated risks factors in Ontario children *Sci. Tot. Env.*, 71 477-483

Osweiler G D , T L Carson, W B Buck, G A Van Gelder eds. 1985 *Clinical and diagnostic veterinary toxicology*, Dubuque Kendall Hunt Publishing Company

Ott L ed 1988 *An introduction to statistical methods and data analysis, 3rd edition* Boston PWS-Kent Publishing Company

Paglinca A., G J Mufti, D Baldwin, A N Lestas, R M Wallis, A.J. Bellingham 1990· Lead poisoning clinical, biochemical, and haematological aspects of a recent outbreak *J Clin Path* , 43 277-281

Parsons P J , A A Reilly, A Hussain 1991. Observational study of erythrocyte protoporphyrin screening test for detecting low lead exposure in children· impact of lowering the blood lead action threshold *Clin Chem* , 37, (2) 216-225

Pinault L , G. Milhaud 1983 Evaluation of subclinical lead poisoning in dairy cattle in *Veterinary Pharmacology and Toxicology* edited by Ruckebush Y , Toutain P L , Koritz G D 715-724 Boston MTP Press Limited

Poulos L , S Qammaz, S Athanaselis, C Maravelias, A Koutselinis. 1986. Statistically significant hematopoietic effects of low blood lead levels *Arch Environ. Health*, 41 (6) 384-386

Rabinowitz M B , D C Bellinger 1988 Soil lead-Blood lead relationship among Boston children *Bull Environ Contam Toxicol*, 41: 791-797

Roberts R D , M S Hohnson 1978 Lead contamination of small mammals from abandonned metalliferous mines *Environ Pollut* , 15 61-69

Rolton C E., B J Horton, D A Pass 1978 Evaluation of tests for the diagnosis of lead exposure in sheep *Aust Vet. J.*, 54 393-397

Scharding N N , F W Oehme 1973 The use of animal models for comparative studies of lead poisoning *Clin. Tox* , 6 (3) 419-424

Scheuhammer A M 1987 Erythrocyte ∂-aminolevulinic acid dehydratase in birds II. The effects of lead exposure in vivo *Toxicol* , 45 165-175

Schilling R J , R.P Bain. 1988 Prediction of children's blood lead levels on the basis of household specific soil lead levels *Am J Epid* , 128 (1) 197-205

Schütz A , S Skerfving, S Mattson, O Christoffersson, L Ahlgren 1987 Lead in vertebral bone biopsies from active and retired lead workers *Arch. Environ Health* , 42 (6) 340-346

Schwartz J , R. Levin 1991 The risk of lead toxicity in homes with lead paint hazard. *Environ Res* , 54 1-7

Silbergeld E K 1990 Toward the twenty-first century lessons from lead and lessons yet to learn *Env Health Persp* , 86· 191-196

Soil Conservation Service, US Department of Agriculture 1986. *Soil survey of Madison County, Illinois*, Washington D.C US Governement Printing Office

Steel R G D., J H Torrie eds. 1980 *Principles and procedures of statistics. A biometrical approach 2nd edition*, New York. McGraw-Hill Publishing Company

Steele M J , B D Beck, B L Murphy, H S. Strauss 1990 Assessing the contribution from lead in mining wastes to blood lead *Regul Toxicol Pharmacol* , 11: 158-190

Thomas C W., J L Rising, J K. Moore. 1976 Blood lead concentrations of children and dogs from 83 Illinois families *J.A.V.M.A* , 169 (11) 1237-1240

Watson A D J 1983 Plumbism in pets and people *Med. J. Aust* , 1 (6) 254

White D J 1977 Histochemical and histological effects of lead on the liver and kidney of the dog *Br J. Exp Path* , 58 101-112

Wielopolski L , K.J Ellis, A N Vaswani, S H. Cohn, A. Greenberg, J.B Puschett, D K Parkinson, D E. Fetterolf, P J. Landrigan 1986 *In vivo* bone lead measurements· a rapid monitoring method for cumulative lead exposure *Am. J. Ind Med.*, 9 221-226

Wigfield D C , J P. Farant. 1981 Assay of ∂-aminolevulinate dehydratase in 10 µl of blood *Clin Chem* , 27 (1) 100-103

Zimdahl R L , D E Koeppe 1977 Uptake by plants in *Lead in the environment* edited by Boggess W R 99-105 Washington D.C National Science Foundation

Zook B C. 1978 Lead intoxication in urban dogs in *Toxicity of Heavy Metals in the Environment* edited by Oehme F W 179-190 New York: Marcel Dekker
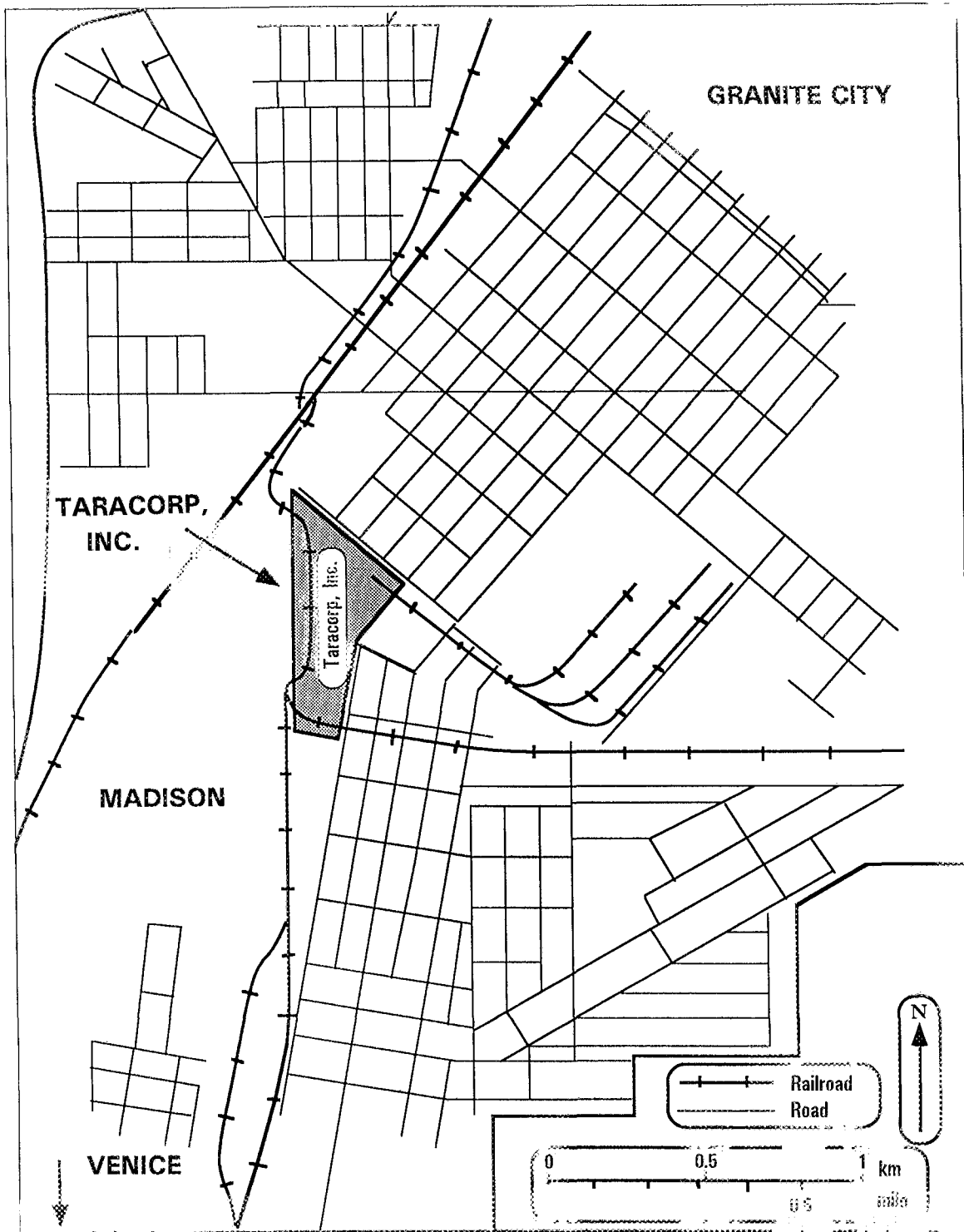
Figure 1. Map of Granite City and Madison, Madison County, Illinois showing the Taracorp, Inc site

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