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LEAD PAINT INGESTION STUDY

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FINAL REPORT
14 September 1973

Contract No. 62-W-62GC&MPC
MRI Project No. 3729-8

For

National Paint and Coatings Association
1500 Rhode Island Avenue, N.W.
Washington, D.C. 20005

Attn: Mr. Royal A. Brown

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PREFACE

This report was prepared at Midwest Research Institute, 425 Volker Boulevard, Kansas City, Missouri 64110, under Contract No. 62-W-62GC&NPC, MRI Project No. 3729-B, "Lead Paint Ingestion Study." The research was sponsored by the National Paint and Coatings Association, 1500 Rhode Island Avenue, N.W., Washington, D.C. 20005. Dr. John P. Frawley, Chief Toxicologist, Hercules, Inc., Wilmington, Delaware 19899, was the project monitor.

The research was conducted in the Biological Sciences Division, under the direction of Dr. W. B. House from 1 December 1972 through 31 July 1973. Dr. Thomas R. Castles, Principal Pharmacologist, was the principal investigator, assisted by Dr. Jaime L. Sanyer, Associate Pathologist, and Mrs. Jane Koch, Biology Research Assistant. Dr. James L. Spigarelli, Senior Chemist supervised the lead analysis with the assistance of Mrs. Hopa M. Miller, Assistant Chemist.

Approved for:

MIDWEST RESEARCH INSTITUTE

W. B. House, Director
Biological Sciences Division

14 September 1973

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white lead

I. INTRODUCTION

Few persons will disagree that old lead-based paint presents a ^{potential} ~~serious and unnecessary health hazard to young children~~. As a result of reports by Kehoe,¹ Chisholm,² and King,³ medical researchers, paint manufacturers and legislators have recognized the seriousness of this problem and are acting to establish safe concentrations of lead in paint. To do this, they have voluminous reports on clinical observations and animal research from which to draw. Unfortunately, most of this information is based upon the old ~~lead-based paints of 1900 and 1910, which are not representative of the paint formulations on today's market.~~

potential health hazard to young children if ingested

Before safe concentrations of lead in paint can be intelligently established, we must evaluate the toxicity of the lead as it exists currently in modern paints. It was the purpose of this study to evaluate the toxicity in rats produced by modern paints containing lead octoate, lead chromate or lead carbonate and to compare them to an old paint formulation typical of those responsible for lead poisoning. The results are presented in the following pages.

Lead based paint Fish-Spacer

II. METHODS

A. Preparation of Paint Films Containing Different Concentrations of Lead

Paint films, ^{from freshly prepared paint} without added lead and added lead compounds in the form of lead octoate, lead chromate, or lead carbonate were supplied by members of the National Paint and Coatings Association. Paints which contained lead octoate, lead chromate (medium yellow) ~~or lead carbonate~~ were prepared using a flat alkyl enamel formula based upon a TI-R-256D Type I Class B alkyl. The flat alkyl paint without added lead was used for control. The percent of lead in each sample was calculated on the basis of the nonvolatile material. Dispersion was accomplished with a Cowles Dissolver and the pigment volume concentration was held at one level. The paints were placed in pans and allowed to air dry. This was followed by forced air drying at 120°F to volatilize any remaining solvent. Paint films were ground, sieved, and chips ranging from 0.5 to 1.0 mm in size were used for this study. This chip size was selected on the basis of a preliminary rat feeding study which established that rats would selectively eat around larger sized chips.

*0.1 d 0.0803
at varying conc.
Compared to old paint
Paint*

^{but would eat selected sized chips}
The concentrations of lead in the different paint films were determined independently by DeSoto Incorporated, the Sharvin-Williams Company and Midwest Research Institute, using Atomic Absorption Spectrophotometry.

In addition a freshly prepared sample of an old lead based paint formula (white lead in oil) was included.

collected from waste of old shellings,

Sample of old lead-based paint, ^{lead} obtained from the U.S. Department of Commerce, National Bureau of Standards, Washington, D.C. This paint had been pulverized and sieved through 325 mesh screen (0.05-0.08 mm size) and contained 11.87% lead by weight. This sample will be referred to as "NBS lead paint" in this report.

B. Preparation of Diets

Diets were prepared by mixing paint ^{Chips} with Purina Rat Chow mash in the concentration of 0.1% (weight/weight). This was accomplished by first preparing a 10% concentrate (paint film/food, w/w) in a high-speed twin shell mixer. This concentrate was then added to the appropriate amount of Purina Rat Chow mash to give a final concentration of 0.1% (paint film/food, w/w) and mixed for 10 min in a bulk mixer.

Each diet was prepared three times during the experiment and samples of each of these preparations were assayed for lead content.

C. Experimental Procedure

Two hundred weanling (40-60 gm) Charles River rats (100 males and 100 female rats) were used for this study. Upon arrival rats were housed individually in air conditioned quarters in polycarbonate cages containing hardwood bedding and filter tops. After 5-7 days of equilibration, all rats were assigned one of the following diets.

1. Rat chow plus paint ^{Chips} film without added lead (control)
2. Rat chow plus paint ^A film containing 0.08% lead as lead octoate
3. Rat chow plus paint ^A film containing 0.53% lead as lead octoate
4. Rat chow plus paint ^B film containing 2.05% lead as lead octoate
5. Rat chow plus paint ^B film containing 0.42% lead as lead chromate
6. Rat chow plus paint ^B film containing 1.95% lead as lead chromate
7. Rat chow plus paint ^B film containing 12.43% lead as lead chromate
8. Rat chow plus paint ^B film containing 66.05% lead as lead carbonate
9. Rat chow plus NBS lead paint containing 11.92% lead ~~as lead carbonate~~ ^{as Carbonate}

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Twenty male and 20 female rats were assigned to the control diet, and 10 males and 10 female rats were assigned to each of the remaining diets. Each diet was fed in a 9-oz wide-mouth glass jar which was secured to the cage. Tap water was available ad libitum during the entire experiment.

Feed consumption was measured twice each week and calculated on a daily basis. The animals were weighed once a week. All rats were observed twice or more each week for toxic signs.

After 4, 8 and 13 weeks, a selected number of male and female rats from each group were placed in metabolism cages for the collection of 24-hr urine samples. A portion of the collected urine was used for urinalysis and the remainder frozen for assay of delta-aminolevulinic acid and coproporphyrin. After urine collection each rat was anesthetized with ether, exsanguinated via the abdominal aorta and bone marrow smears were prepared. Blood samples were heparinized, cooled and used immediately for hematology and enzyme assays. Aliquots of the remaining blood were taken for protoporphyrin and lead assays. After urine and blood samples were obtained, each rat was necropsied and tissue taken for lead analysis ^{or} microscopic examination.

D. Analyses

1. Lead analyses of paint films and diets containing paint films:

a. Paint film: Ten-milligram samples of paint ^{films} containing no lead or 0.08% lead octoate were charred with 3 ml of concentrated nitric acid and dry-ashed at 500°C for 2 hr. The ash was dissolved in 1 ml of aqua regia, diluted to 5 ml with distilled water and this final dilution measured for lead content by atomic absorption.

All other paint ^{films} (10 mg samples) were digested in 15 ml of a mixture of concentrated nitric acid and 37% perchloric acid (2:1, V/V), evaporated and the remaining perchloric acid solution diluted to 25 ml with distilled water. This final dilution was used for atomic absorption spectrophotometry.

b. Diets: One-gram samples of feed were digested in a mixture of concentrated nitric acid and 37% perchloric acid (2:1, V/V) and their final dilutions adjusted to make their lead concentrations within the detection limits of the atomic absorption technique.

2. Analyses performed upon each rat:

a. Hematology:

(1) Hematocrit: Hematocrit was determined in capillary tubes using a microcapillary centrifuge (International Equipment Company, Model MB).

(2) Hemoglobin: Hemoglobin was measured as cyanomethemoglobin.^{4/}

(3) Erythrocyte and leukocyte counts: Total erythrocyte and leukocyte were counted using a Coulter Electronic Particle Counter with 100-u aperture.^{5/}

(4) Reticulocytes: Reticulocytes were counted by the methylene blue method using the Miller disc.^{6/}

(5) Differential leukocyte counts: Wright's stain was used to stain the leukocytes for examination.

(6) Erythrocyte osmotic fragility: Osmotic fragility of erythrocytes was quantitatively determined by subjecting heparinized whole blood to sodium chloride solutions of different osmolarities.^{7/} The concentration of sodium chloride which hemolyzed 50% of the erythrocytes was obtained from a plot of percent hemolysis versus sodium chloride concentration.

b. Body fluid and tissue chemistry:

(1) Plasma protein electrophoretic patterns: Total plasma protein were determined using the Dycal Biuret Reagent (Dycal, Inc., Houston, Texas). The quantity of each plasma protein was determined electrophoretically on cellulose acetate and expressed as a percentage of the total plasma protein.

(2) Erythrocyte- δ -aminolevulinic acid dehydrase (A₂D): δ -Aminolevulinic acid dehydrase activity was determined by the method of Licheman and Feldman.^{8/} This procedure was started 30 min after each blood sample was taken.

(3) Erythrocyte protoporphyrin: Protoporphyrin in erythrocytes was measured by the method of Heller, et al.^{9/} This analysis was performed the day after blood was withdrawn.

(4) Urinary δ -aminolevulinic acid (ALA): Urinary δ -aminolevulinic acid was measured according to the Davis and Andelman^{10/} modification of Mauzerall's and Granick's Method.^{11/} These analyses were performed in subdued light.

(5) Urinary coproporphyrin: Urinary coproporphyrins were determined by the method of Schlanter and Kitchell.^{12/} These analyses were performed in subdued light.

c. Urinalysis:

(1) Urinary protein (albumin): Urinary protein was measured with "Uristix" reagents strips (Ames Company, Elkhart, Indiana).

(2) Microscopic examination of urine: Urine samples were centrifuged, the residues resuspended, and examined microscopically for the presence of erythrocytes and leukocytes under high power field and for casts under low power field.

d. Tissue lead:

(1) Blood: One milliliter of blood was mixed with 1 ml of a mixture of 5% trichloroacetic acid:37% perchloric acid (3:1 v/v). The sample was centrifuged and the supernatant filtered through an AAWF 0.8 μ Millipore filter. The supernate was analyzed for lead with an atomic absorption spectrophotometer using standards prepared in control rat blood.

(2) Other tissues: Bone, liver, kidney, and brain were digested in concentrated nitric acid, evaporated to dryness and reconstituted to the lowest possible volume with 20% nitric acid. These solutions were analyzed for lead by atomic absorption spectrophotometry.

(3) Atomic absorption analysis: Lead concentrations were measured using a Varian-Techtron AA-5 atomic absorption spectrophotometer. Sample solutions were aspirated into an air-acetylene flame and the absorbance was measured at 283.3 nm. Background interference was determined with the use of a hydrogen continuum lamp at 283.3 nm and subtracted from the absorbance obtained at 283.3 nm with the Pb hollow cathode lamp.

E. Pathology

1. Gross pathology: At necropsy, rats were examined for gross abnormalities, their livers, kidneys, spleens, hearts, gonads, thyroids, brains, and adrenals weighed, and the relative organ weights calculated. After weighing, a portion of the liver, kidney and brain were taken for microscopic examination and the rest of each organ was measured for lead content. A femur was removed to be used for the measurement of lead in bone.

2. Microscopic pathology: Bone marrow smears were prepared for a myeloid/erythroid cell count. The following tissues were fixed in buffered neutral 10% formalin: brain, liver, spleen, stomach, small intestine

(duodenum, jejunum, ileum), colon, pancreas, kidneys, urinary bladder, adrenals, thymus, gonad, thyroid (with parathyroid attached), mesenteric salivary gland, lymph nodes, heart, lungs, diaphragm, skeletal muscle, and prostate or uterus.

Tissues from all 13 week rats fed the control, 2.05% lead octoate, 12.43% lead chromate, 66.05% lead carbonate, and the 11.92% NBS lead paint diets were embedded in paraffin, section to a thickness of 6 μ , stained with hematoxylin and eosin and examined for histopathology.

F. Statistical Analyses

Control and treatment values were compared statistically using Dunnett's multiple-comparison test with $P < 0.05$ as the criteria of significance.

III. RESULTS

A. Concentrations of Lead in Paint ^{Chips} Films

The concentrations of lead in the paint ^{Chips} films supplied by the Members of the National Paint and Coatings Association were analyzed for lead content by DeSoto Incorporated, the Sherwin-Williams Company, and Midwest Research Institute (MRI). The results of these analyses are shown in Table 1. The control ^{Chips} which did not contain lead octoate or chromate was found to contain approximately 0.01% lead. There was a reasonable agreement between the different analyses, so an average ppm of lead was computed and used for the actual lead concentration of each paint film. Lead concentrations of the lead paint obtained from the National Bureau of Standards were averaged in a similar manner.

B. Lead Analyses of Diets Containing Different Paint Films

Table 2 shows the lead content of each diet. Purina Rat Chow Mash was found to contain approximately 4 $\mu\text{g}/\text{gm}$ of lead (assuming 0.1 $\mu\text{g}/\text{gm}$ of lead was contributed by the control paint). The μg of lead/ gm of feed which was attributable to each added paint film was reasonably close to its respective theoretical value. The average total μg of lead/ gm of feed for each diet was used for the calculation of weekly and total lead consumption for each rat.

TABLE I

CONCENTRATION OF LEAD IN PAINT FILM

Paint Film	Theoretical Lead Concentration (%)	Measured Lead Concentration		
		Paint Companies (%)	MRI (%)	Average ^{a/} "
Control Paint	0	0.01	< 0.33	0.01
Lead octoate	0.06	0.08	0.07	0.08
Lead octoate	0.50	0.50	0.56	0.53
Lead octoate	2.00	1.90	2.20	2.05
Lead chromate	0.50	0.42	0.41	0.42
Lead chromate	2.00	1.80	2.10	1.95
Lead chromate	15.00	12.37	12.30	12.43
Lead carbonate	64.12	63.20	68.90	66.05
NBS lead paint	-	11.87 ^{b/}	11.98	11.92 ^{c/}

^{a/} Measured by U.S. Department of Commerce, National Bureau of Standards, Washington, D.C.

^{b/} Average of paint companies and MRI values.

^{c/} Average of Bureau of Standards and MRI values.

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TABLE 2

LEAD ANALYSES OF DIETS CONTAINING DIFFERENT PAINT FILMS

<u>Diet</u>	<u>Theoretical^{a/}</u> (<u>ug/gm</u>)	<u>Measured</u>	
		<u>Total^{b/}</u> (<u>ug/gm</u>)	<u>Paint Lead^{c/}</u> (<u>ug/gm</u>)
Control paint plus rat chow	0.1	4.1 (6)	-
Lead octoate (0.08%) plus rat chow	0.8	5.2 (6)	1.1 (6)
Lead octoate (0.53%) plus rat chow	5.3	12.0 (6)	7.9 (6)
Lead octoate (2.05%) plus rat chow	20.5	27.2 (6)	23.1 (6)
Lead chromate (0.42%) plus rat chow	4.2	11.0 (6)	6.9 (6)
Lead chromate (1.95%) plus rat chow	19.5	23.5 (6)	19.4 (6)
Lead chromate (12.43%) plus rat chow	124.3	140.2 (6)	136.1 (6)
Lead carbonate (66.05%) plus rat chow	660.5	516.0 (5)	511.9 (5)
NBS Lead based paint (11.92%) plus rat chow	119.2	124.0 (3)	119.9 (3)

- a/ Theoretical concentration of lead in feed contributed by indicated paint film.
b/ Mean ug of lead/gm feed for number of samples shown in parenthesis.
c/ Mean ug of lead from paint films/gm feed for number of samples shown in parenthesis.

C. Preliminary Feeding Studies

Before beginning this study, a pilot experiment was performed to see if the rats were consuming the lead paint ^{chip} along with their feed. Three rats each were placed on the control diet and the 66.05% lead carbonate diet. After 48 hr, feces were collected and ~~their~~ lead content measured. Feces from rats on the control diet contained 11.5 μ g of lead/gm feces while feces from rats fed the 66.05% lead carbonate diet contained 3,683 μ g of lead/gm feces. Thus, rats did consume the paint ^{chip} along with their feed.

D. Gross Observations, Feed Consumptions and Body Weights

During the entire study only two rats had remarkable changes. One female rat on 2.05% lead octoate developed an abscess on her left shoulder during the ninth treatment week and one female on 66.05% lead carbonate developed abscessed hind feet in the 10th week and chew her toes off.

The feed consumption of male and female rats are shown in Figures 1 and 2, respectively. Except for the rats fed the diet containing 11.92% lead as NBS lead paint, all groups consumed feed at the same rate as the control group throughout the entire experiment. The reason the 11.92% NBS lead paint group ate significantly less initially, was that they were started a month after the other rats and were initially smaller. Since this group was consuming feed at the same rate as the control group by 4 weeks, we consider their initial food consumption normal also (for their size).

The body weight gains for each group of rats are shown in Figures 3 and 4. As mentioned above, the rats on the 11.92% NBS lead paint diet were small initially but became similar to controls by either the 4th (females) or 8th week (males). Throughout the entire period the male rats in the other treatment groups gained weight at a normal rate. The female rats did show a change in body weights during the first 8 weeks of feeding which appears related to the concentration of lead octoate. After 4 weeks of feeding, rats in the 2.05% lead octoate group weighed significantly less than control. The pattern was the same at 8 weeks. After 12 weeks their average body weights still exhibited the same pattern, but the 2.05% lead octoate group was not significantly different from control. This was due to fewer animals and a slight increase in variability.

*Each bar represents the mean \pm std error
of the number of rats indicated
4 to 20 rats.*

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Figure 2
 Feed Consumption of Female Pigs Fed Different Concentrations of Lead in Palm Oil

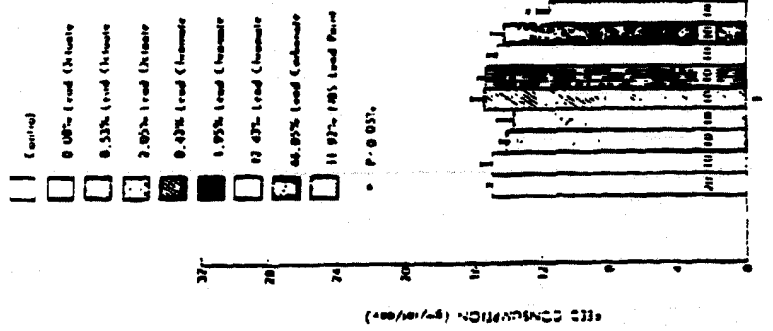


Figure 3

Diagram of Able, Base, and Outboard
Concentrations of Lead in Paint Film

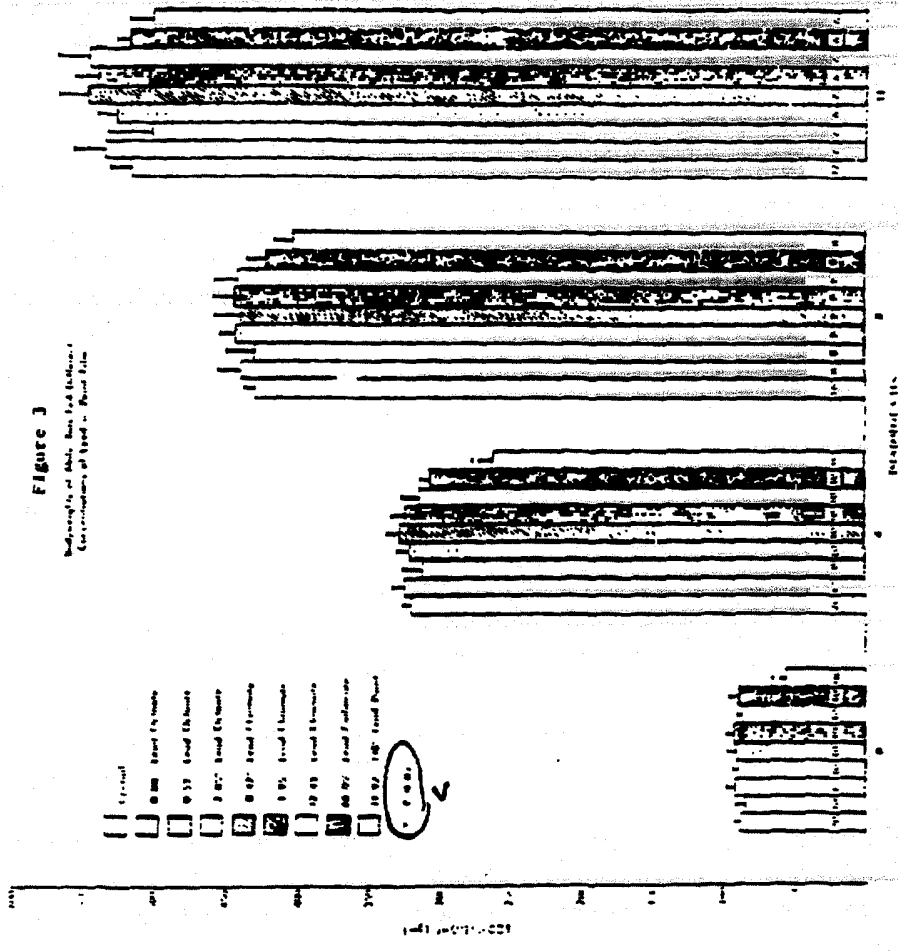
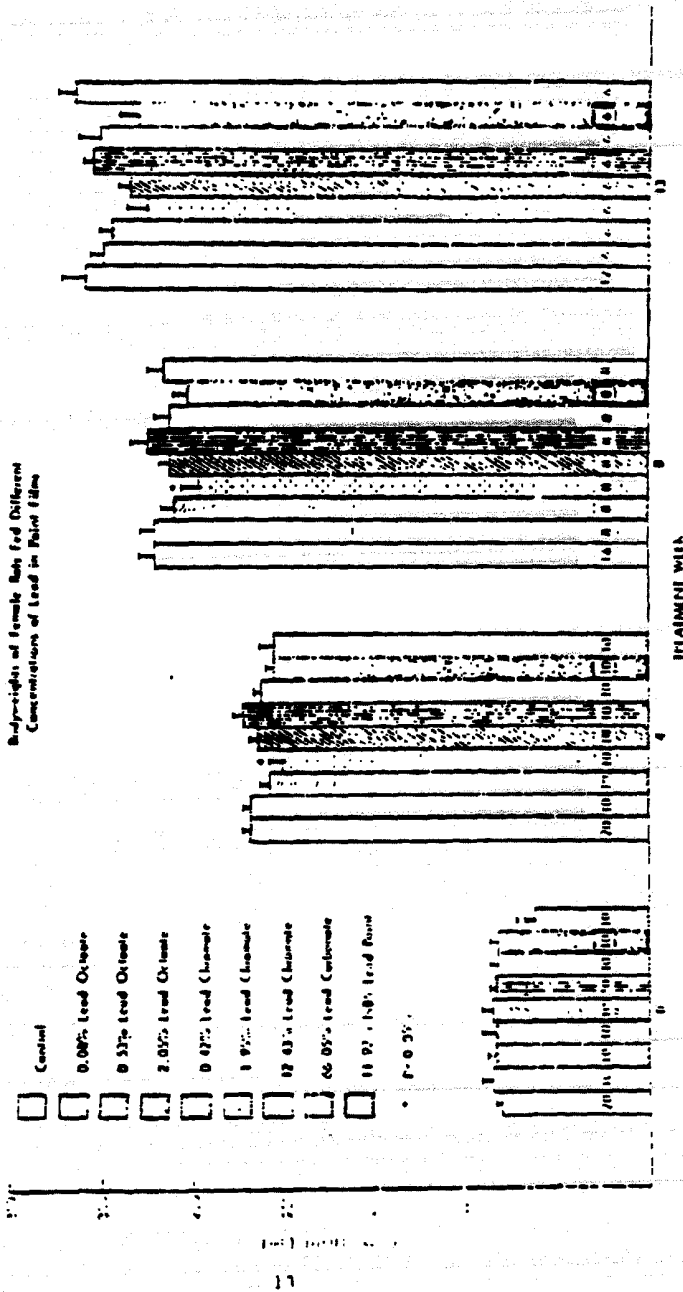


Figure 4
Subjects of Female Rats Fed Different
Concentrations of Lead in Paint Film



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Lead

E. Weekly and Total Lead Consumption

The weekly and total lead consumption during the experiment were calculated on the basis of the total lead/diet and amount of each diet eaten by each rat. These calculations are shown in Tables 3 and 4. During the 13th week period, the control group consumed approximately 105 ug of lead/day, while rats eating 2.05% lead octoate, 12.43% lead chromate, 66.05% lead carbonate, and 11.92% NBS lead paint consumed an average of 786.9, 3,591.1, 13,435.8, and 3,284.3 ug of lead/day, respectively. Using the average body weights of rats surviving 13 days, the rats in the control, 2.05% lead octoate, 12.43% lead chromate, 66.05% and 11.92% NBS lead paint groups consumed 245.2; 1,957.5; 8,469.6; 34,450.8; and 7,804.7 ug of lead/kg/day, respectively.

To
be
used
for
analysis

F. Hematology of Rats Fed Paint Films Containing Different Concentrations of Lead

The results of the hematology of rats fed paint films containing different concentrations of lead are shown in Tables 5-13. No differences were observed in the erythrocyte count, reticulocyte count, hematocrit, leukocyte count, differential leukocyte count, and the erythrocyte osmotic fragility.

G. Tissue and Fluid Chemistry of Rats Fed Paint Films Containing Different Concentrations of Lead

Tables 14-22 show the tissue and fluid chemistry of rats fed paint films containing different concentrations of lead. The serum proteins, erythrocyte protoporphyrin, urinary coproporphyrin, and urinary delta-aminolevulinic acid were not altered by any of the diets.

The activity of the erythrocyte enzyme, delta-aminolevulinic acid dehydrase (ALAD), in the control, lead octoate (0.08%, 0.53%, and 2.05%) and lead chromate (0.25%, 1.95% and 12.43%) groups did not differ throughout the experiment (Tables 23). ALAD activity was depressed in rats fed 66.05% lead carbonate and 11.92% NBS lead paint. At 4 weeks there was a depression of 56% and 59% in these two groups, respectively. At 8 weeks the ALAD activity was depressed in the 66.05% lead carbonate group, but the ALAD activity in the NBS lead paint group was not significantly different from control. At this time a sex difference was observed in both of these groups. The ALAD activity in the male rats remained depressed at the 4-week levels while the ALAD activities of the female rats returned to control levels. This sex difference may be linked to the fact that these female rats had matured and were probably beginning their menstrual cycles.

(Table 21 & 22)

TABLE 6
 MONTHLY AND QUARTERLY INVESTMENT IN THE UNITED STATES, 1957-1967

Category	Investment, \$ mil.												Total	Percent of total		
	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968				
Government	1,100	1,100	1,100	1,100	1,100	1,100	1,100	1,100	1,100	1,100	1,100	1,100	1,100	1,100	1,100	1,100
Non-government	1,100	1,100	1,100	1,100	1,100	1,100	1,100	1,100	1,100	1,100	1,100	1,100	1,100	1,100	1,100	1,100
Total	2,200	2,200	2,200	2,200	2,200	2,200	2,200	2,200	2,200	2,200	2,200	2,200	2,200	2,200	2,200	2,200
Percent of total	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50

1. The data are preliminary estimates for the months of July through September.
 2. The data are preliminary estimates for the months of October, November, and December.
 3. The data are preliminary estimates for the months of January, February, and March.
 4. The data are preliminary estimates for the months of April, May, and June.

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TABLE 5

HENATOLOGY OF RATS FED PAINT ^{Chloro}
CONTAINING NO LEAD

Analyses	Treatment Week		
	4 (N=8) ^{a/}	8 (N=8)	13 (N=24)
Erythrocytes (x 10 ⁶ /mm ³)	6.17 ± 0.14 ^{b/}	6.33 ± 0.19	6.42 ± 0.29
Reticulocytes, %	1.5 ± 0.7	0.8 ± 0.3	1.4 ± 0.1
Hematocrit, vol, %	46.1 ± 0.8	44.6 ± 1.2	44.6 ± 0.3
Hemoglobin, gm, %	14.0 ± 0.3	14.6 ± 0.3	16.0 ± 0.1
Leukocytes (x 10 ³ /mm ³)	5.0 ± 0.5	7.6 ± 1.3	8.0 ± 0.6
Neutrophils, %	11.8 ± 2.9	21.7 ± 5.6	13.1 ± 1.5
Lymphocytes, %	86.3 ± 3.3	75.4 ± 5.3	84.1 ± 1.6
Sands, %	0.3 ± 0.2	0	0.1 ± 0.1
Eosinophils, %	0.9 ± 0.4	1.3 ± 0.4	0.3 ± 0.2
Basophils, %	0	0	0
Monocytes, %	1.1 ± 0.6	1.6 ± 0.6	2.1 ± 0.4
Atypical, %	0	0	0
Nucleated RBC, %	0	0	0.1 ± 0.1
Erythrocyte osmotic fragility [NaCl] ^{c/}	0.381 ± 0.004	0.391 ± 0.008	0.400 ± 0.004

^{a/} Number of rats per period.

^{b/} Mean ± standard error.

^{c/} Concentration of NaCl that hemolyzed 50% of the erythrocytes.

TABLE 6

clino
HEMATOLOGY OF RATS FED PAINI
CONTAINING 0.08% LEAD AS LEAD OCTOATE

Analyses	Treatment Week		
	4 (N=6) ^{a/}	8 (N=6)	13 (N=12)
Erythrocytes ($\times 10^6/\text{mm}^3$)	6.14 \pm 0.32 ^{b/}	6.33 \pm 0.09	5.92 \pm 0.39
Reticulocytes, %	0.9 \pm 0.5	1.0 \pm 0.5	1.4 \pm 0.2
Hematocrit, vol. %	41.3 \pm 0.9	46.0 \pm 0.7	43.0 \pm 0.5
Hemoglobin, gm %	14.1 \pm 0.4	15.4 \pm 0.2	14.7 \pm 0.8
Leukocytes ($\times 10^3/\text{mm}^3$)	5.1 \pm 0.8	5.5 \pm 0.7	7.7 \pm 0.9
Neutrophils, %	24.5 \pm 1.6	20.3 \pm 4.7	16.3 \pm 1.7
Lymphocytes, %	74.3 \pm 1.8	76.3 \pm 4.7	80.9 \pm 1.8
Bands, %	0	0	0.3 \pm 0.2
Eosinophils, %	0.8 \pm 0.3	1.5 \pm 0.6	0.7 \pm 0.3
Basophils, %	0	0	0
Monocytes, %	0.5 \pm 0.5	2.0 \pm 0.8	1.9 \pm 0.5
Atypical, %	0	0	0
Nucleated RBC, %	0	0	0
Erythrocyte osmotic fragility [NaCl] ^{c/}	0.381 \pm 0.005	0.410 \pm 0.007	0.395 \pm 0.005

^{a/} Number of rats per period.

^{b/} Mean \pm standard error.

^{c/} Concentration of NaCl that hemolyzed 50% of the erythrocytes.

TABLE 7

change
HEMATOLOGY OF RATS FED PAINT
CONTAINING 0.53% LEAD AS LEAD OCTOATE

Analyses	Treatment Week		
	4 (N=6) ^{a/}	8 (N=6)	13 (N=10)
Erythrocytes ($\times 10^6/\text{mm}^3$)	6.27 = 0.2 ^{b/}	6.04 = 0.31	5.6 = 0.4
Reticulocytes, %	0.9 = 0.7	0.9 = 0.4	1.6 = 0.2
Hematocrit, vol. %	42.3 = 0.7	43.8 = 0.5	43 = 0.7
Hemoglobin, gm %	14.2 = 0.2	14.9 = 0.3	15.3 = 0.3
Leukocytes ($\times 10^3/\text{mm}^3$)	5.0 = 1.4	7.5 = 2.8	8.3 = 1.0
Neutrophils, %	15.8 = 3.8	19.3 = 3.8	16.2 = 1.9
Lymphocytes, %	83.0 = 4.4	77.5 = 3.8	81.4 = 1.8
Bands, %	0	0	0.1 = 0.1
Eosinophils, %	0.8 = 0.3	1.0 = 0.4	0.8 = 0.3
Basophils, %	0	0	0
Monocytes, %	0.5 = 0.5	2.3 = 0.5	1.6 = 0.3
Atypical, %	0	0	0
Nucleated RBC, %	0	0	0
Erythrocyte osmotic fragility [NaCl] ^{c/}	0.383 = 0.006	0.388 = 0.012	0.401 = 0.006

a/ Number of rats per period.

b/ Mean = standard error.

c/ Concentration of NaCl that hemolyzed 50% of the erythrocytes.

TABLE 8

Chips
 HEMATOLOGY OF RATS FED PAINT ~~CHIPS~~
 CONTAINING 2.35% LEAD AS LEAD OCTOATE

Analysis	Treatment Week		
	4 (N=6) ^{a/}	8 (N=6)	13 (N=12)
Erythrocytes ($\times 10^6/\text{mm}^3$)	6.30 \pm 0.7 ^{b/}	6.46 \pm 0.08	6.72 \pm 0.42
Reticulocytes, %	1.1 \pm 0.6	0.7 \pm 0.1	2.0 \pm 0.6
Hematocrit, vol. %	41.8 \pm 0.5	45.0 \pm 0.4	43.4 \pm 0.8
Hemoglobin, gm %	14.4 \pm 0.2	15.5 \pm 0.2	15.6 \pm 0.3
Leukocytes ($\times 10^3/\text{mm}^3$)	5.1 \pm 1.1	6.7 \pm 1.7	8.1 \pm 0.7
Neutrophils, %	13.5 \pm 3.0	13.0 \pm 2.1	14.1 \pm 2.6
Lymphocytes, %	85.8 \pm 3.2	85.0 \pm 2.3	82.8 \pm 2.8
Bands, %	0	0	0
Eosinophils, %	0.8 \pm 0.5	0.3 \pm 0.3	0.9 \pm 0.3
Basophils, %	0	0	0
Monocytes, %	0	1.8 \pm 0.9	2.2 \pm 0.7
Atypical, %	0	0	0
Nucleated RBC, %	0	0	0
Erythrocyte osmotic fragility [NaCl] ^{c/}	0.381 \pm 0.006	0.399 \pm 0.008	0.393 \pm 0.006

^{a/} Number of rats per period.

^{b/} Mean \pm standard error.

^{c/} Concentration of NaCl that hemolyzed 50% of the erythrocytes.

TABLE 9

change
HEMATOLOGY OF RATS FED PAINT PASTE
CONTAINING 0.5% LEAD AS LEAD CHROMATE

Analyses	Treatment Week		
	4 (N=6) ^{a/}	8 (N=6)	13 (N=12)
Erythrocytes ($\times 10^6/\text{mm}^3$)	6.71 \pm 0.16 ^{b/}	6.38 \pm 0.16	6.6 \pm 0.3
Reticulocytes, %	0.9 \pm 0.8	0.8 \pm 0.2	1.6 \pm 0.2
Hematocrit, vol. %	43.3 \pm 0.6	45.0 \pm 1.1	43.6 \pm 0.7
Hemoglobin, gm %	14.7 \pm 0.4	15.1 \pm 0.3	15.6 \pm 0.3
Leukocytes ($\times 10^3/\text{mm}^3$)	5.1 \pm 0.6	5.1 \pm 0.5	6.9 \pm 0.7
Neutrophils, %	8.5 \pm 1.7	19.0 \pm 2.0	14.3 \pm 2.1
Lymphocytes, %	90.3 \pm 2.0	79.5 \pm 1.3	83.4 \pm 2.0
Bands, %	0	0	0
Eosinophils, %	0	0.8 \pm 0.8	1.2 \pm 0.4
Basophils, %	0	0	0
Monocytes, %	1.3 \pm 0.8	0.8 \pm 0.8	1.2 \pm 0.4
Atypical, %	0	0	0
Nucleated RBC, %	0	0.3 \pm 0.3	0
Erythrocyte osmotic fragility, [NaCl] ^{c/}	0.383 \pm 0.003	0.395 \pm 0.12	0.392 \pm 0.007

^{a/} Number of rats per period, except where indicated otherwise.

^{b/} Mean \pm standard error.

^{c/} Concentration of NaCl that hemolyzed 50% of the erythrocytes.

TABLE 10

هیند
 HEMATOLOGY OF RATS FED PAINT
 CONTAINING 1.95% LEAD AS LEAD CHROMATE

Analyses	Treatment Week		
	A (N=6) ^{a/}	B (N=6)	C (N=6)
Erythrocytes ($\times 10^6/\text{mm}^3$)	6.17 = 0.05 ^{b/}	6.21 = 0.13	6.37 = 0.52
Reticulocytes, %	0.8 = 0.4	0.8 = 0.3	1.2 = 0.2
Hematocrit, vol. %	40.8 = 0.6	44.3 = 0.3	44.1 = 0.7
Hemoglobin, gm %	13.9 = 0.2	15.3 = 0.3	16.2 = 0.4
Leukocytes ($\times 10^3/\text{mm}^3$)	4.9 = 0.8	6.1 = 1.2	8.2 = 1.0
Neutrophils, %	10.0 = 2.4	18.5 = 6.6	11.4 = 2.3
Lymphocytes, %	92.0 = 1.8	80.5 = 6.6	85.9 = 2.2
Bands, %	0	0	0
Eosinophils, %	0.5 = 0.3	0.3 = 0.3	1.5 = 0.5
Basophils, %	0	0	0
Monocytes, %	0	0.8 = 0.3	1.2 = 0.3
Atypical, %	0	0	0
Nucleated RBC, %	0	0	0
Erythrocyte osmotic fragility, [NaCl] ^{c/}	0.383 = 0.007	0.385 = 0.007	0.404 = 0.005

^{a/} Number of rats per period.

^{b/} Mean = standard error.

^{c/} Concentration of NaCl that hemolyzed 50% of the erythrocytes.

TABLE 11

Chrys
HEMATOLOGY OF RATS FED PAINT ~~CONTAINING 10.0% LEAD AS LEAD CHROMATE~~

Analyses	Treatment Week		
	4 (N=6) ^{a/}	8 (N=4)	12 (N=12)
Erythrocytes ($\times 10^6/\text{mm}^3$)	6.32 \pm 0.14 ^{b/}	6.23 \pm 0.18	6.61 \pm 0.39
Reticulocytes, %	1.95 \pm 1.28	0.9 \pm 0.1	1.6 \pm 0.2
Hematocrit, vol. %	41.3 \pm 1.1	43.8 \pm 0.5	44.1 \pm 0.7
Hemoglobin, gm %	13.9 \pm 0.4	15.2 \pm 0.1	15.8 \pm 0.2
Leukocytes ($\times 10^3/\text{mm}^3$)	4.8 \pm 0.5	5.3 \pm 1.8	7.6 \pm 0.6
Neutrophils, %	21.5 \pm 6.3	15.0 \pm 2.1	12.8 \pm 1.6
Lymphocytes, %	78.0 \pm 6.0	82.8 \pm 2.0	84.8 \pm 1.7
Bands, %	0	0	0.1 \pm 0.1
Eosinophils, %	0.5 \pm 0.5	1.0 \pm 0	1.0 \pm 0.4
Basophils, %	0	0	0
Monocytes, %	0	1.3 \pm 0.3	1.3 \pm 0.3
Atypical, %	0	0	0
Nucleated RBC, %	0	0.3 \pm 0.3	0
Erythrocyte osmotic fragility [NaCl] ^{c/}	0.384 \pm 0.007	0.385 \pm 0.010	0.396 \pm 0.006

^{a/} Number of rats per period.

^{b/} Mean \pm standard error.

^{c/} Concentration of NaCl that hemolyzed 50% of the erythrocytes.

TABLE 12

HEMATOLOGY OF RATS FED PAINT
 CONTAINING 86.0% LEAD AS LEAD CARBONATE

Analyses	Treatment Week		
	4 (N=3) ^{a/}	8 (N=4)	13 (N=12)
Erythrocytes ($\times 10^6/\text{mm}^3$)	5.94 \pm 0.56 ^{b/}	6.13 \pm 0.06	6.60 \pm 0.37
Reticulocytes, %	0.4 \pm 0.2	1.1 \pm 0.3	2.9 \pm 1.3
Hematocrit, vol. %	41.3 \pm 0.9	46.0 \pm 1.5	46.7 \pm 1.2
Hemoglobin, gm %	13.9 \pm 0.5	15.0 \pm 0.2	15.6 \pm 0.6
Leukocytes ($\times 10^3/\text{mm}^3$)	4.3 \pm 1.2	5.0 \pm 0.9	7.7 \pm 0.5
Neutrophils, %	14.3 \pm 4.1	15.0 \pm 4.1	15.2 \pm 2.6
Lymphocytes, %	82.0 \pm 5.6	86.0 \pm 4.2	82.7 \pm 2.7
Bands, %	0	0	0.2 \pm 0.1
Eosinophils, %	0.7 \pm 0.7	0.5 \pm 0.5	0.9 \pm 0.3
Basophils, %	0	0	0
Monocytes, %	3.0 \pm 2.0	0.5 \pm 0.3	1.0 \pm 0.3
Atypical, %	0	0	0
Nucleated RBC, %	0	0	0.1 \pm 0.1
Erythrocyte osmotic fragility [NaCl] ^{c/}	0.388 \pm 0.009	0.394 \pm 0.012	0.397 \pm 0.005

^{a/} Number of rats per period.

^{b/} Mean \pm standard error.

^{c/} Concentration of NaCl that hemolyzed 50% of the erythrocytes.

TABLE 13

TOXICOLOGY OF RATS FED RES LEAD
DIET CONTAINING 11.9% LEAD

Treatment Week		
4 (N=12)	8 (N=6)	13 (N=12)
5.72 ± 0.15 ^{h/}	4.49 ± 0.83	5.63 ± 0.34
2.5 ± 0.3	1.0 ± 0.4	1.3 ± 0.1
39.7 ± 0.8	42.8 ± 1.1	42.9 ± 0.4
13.6 ± 5/	14.7 ± 0.3	14.7 ± 0.1 ←
9.7 ± 1.4	6.7 ± 1.2	7.0 ± 0.5
9.5 ± 2.1	7.0 ± 1.7	14.2 ± 2.1
90.2 ± 2.3	92.0 ± 2.1	83.6 ± 2.2
0.3 ± 0.3	0	0
0	0	1.4 ± 0.4
0	0	0
0	1.0 ± 0.7	0.8 ± 0.3
0	0	0
0	0	0.1 ± 0.1
0.389 ± 0.006	0.412 ± 0.006	0.408 ± 0.005

h/ = period, except where indicated otherwise.

5/ = ...

← = ... that hemolyzes 50% of the erythrocytes.

TABLE 14

China
TISSUE AND FLUID CHEMISTRY OF RATS FED PAINT
CONTAINING NO LEAD

Analyses	Treatment Week		
	4 (N=8) ^{a/}	8 (N=8)	13 (N=24)
Serum electrophoresis			
Albumin, %	43 ± 1 ^{b/}	43 ± 2	48 ± 1
Alpha 1 globulin, %	28 ± 1	23 ± 1	21 ± 1
Alpha 2 globulin, %	5 ± 1	5 ± 1	5 ± 1
Beta globulin, %	20 ± 1	20 ± 1	21 ± 1
Gamma globulin, %	6 ± 1	10 ± 1	6 ± 1
Total protein, %	5.4 ± 0.1	6.2 ± 0.2	6.3 ± 0.1
Albumin/globulin ratio	0.76 ± 0.03	0.77 ± 0.07	0.93 ± 0.04
Erythrocyte			
ALAD, μmol. PBG/	Males: 23.2 ± 2.3 ^{c/}	15.1 ± 2.3 ^{e/}	14.5 ± 1.4 ^{d/}
100 ml RBC/hr	Females: 16.6 ± 3.1 ^{e/}	16.3 ± 2.5 ^{e/}	13.4 ± 0.7 ^{d/}
	Total: 19.9 ± 2.2	15.8 ± 1.5	15.0 ± 1.0
Protoporphyrin,	19.6 ± 1.6	23.5 ± 1.9	29.2 ± 2.0
μg/100 ml RBC			
Urine			
Coproporphyrin,	2.5 ± 1.2	3.3 ± 7.4	6.0 ± 1.9
μg/24 hr			
ALA,	78.0 ± 7.4	83.3 ± 11.0	43.4 ± 5.0
μg/24 hr			

^{a/} Number of rats per period, except where indicated otherwise.

^{b/} Mean ± standard error.

^{c/} Four rats.

^{d/} Twelve rats.

TABLE 15

charts
TISSUE AND FLUID CHEMISTRY OF RATS FED PAINT
CONTAINING 0.35% LEAD AS LEAD OXIDE

Analyses	Treatment Week		
	4 (N=6) ^{a/}	8 (N=6)	13 (N=10)
Serum electrophoresis			
Albumin, %	40 = 1 ^{b/}	44 = 3	48 = 1
Alpha 1 globulin, %	26 = 1	20 = 2	20 = 1
Alpha 2 globulin, %	5 = 1	4 = 1	5 = 1
Beta globulin, %	21 = 1	20 = 1	22 = 1
Gamma globulin, %	8 = 1	12 = 1	7 = 1
Total protein, %	5.9 ± 0.1	6.3 ± 0.2	6.2 ± 0.1
Albumin/globulin ratio	0.66 ± 0.02	0.79 ± 0.08	0.93 ± 0.04
Erythrocytes			
ALAD, umol. PBG/ 100 ml RBC/hr	Males: 24.8 ± 7.7 ^{c/}	14.9 ± 1.3 ^{c/}	12.0 ± 2.2 ^{d/}
	Females: 19.5 ± 4.4 ^{c/}	18.7 ± 0.3 ^{c/}	16.1 ± 1.3 ^{d/}
	Total: 22.2 ± 3.9	16.8 ± 1.2	14.0 ± 1.4
Protoporphyrin, ug/100 ml RBC	28.4 ± 2.4	24.2 ± 1.6	22.8 ± 2.5
Urine			
Coproporphyrin, ug/24 hr	1.2 ± 0.2	4.8 ± 2.4	2.9 ± 1.4
ALA, ug/24 hr	86.4 ± 16.6	107.6 ± 34.1	35.0 ± 6.7

^{a/} Number of rats per period, except where indicated otherwise.

^{b/} Mean ± standard error.

^{c/} Two rats.

^{d/} Six rats.

*RBC ?
Red Blood Cell.*

TABLE 16

**TISSUE AND BODY FLUID CHEMISTRY OF RATS FED PAINT
PASTE CONTAINING 0.53% LEAD AS LEAD OCTOATE**

Analyses	Treatment Week		
	0 (No. 12) ^{a/}	6 (No. 6)	13 (No. 12)
Serum electrophoresis			
Albumin, %	41 = 1 ^{b/}	41 = 4	50 = 1
Alpha 1 globulin, %	26 = 1	23 = 3	20 = 1
Alpha 2 globulin, %	5 = 1	6 = 2	4 = 1
Beta globulin, %	21 = 1	20 = 1	20 = 1
Gamma globulin, %	8 = 1	11 = 2	7 = 1
Total protein, %	5.7 = 0.1	6.3 = 0.1	6.0 = 0.1
Albumin/globulin ratio	0.68 ± 0.04	0.70 ± 0.13	1.00 ± 0.07
Erythrocytes			
ALAD, umol. PBC/ 100 ml RBC/hr	Males: 21.4 = 6.3 ^{c/} Females: 15.5 = 2.7 ^{e/} Total: 18.4 = 3.3	10.3 = 0.8 ^{c/} 15.3 = 0.2 ^{e/} 12.8 = 1.5	12.5 = 0.7 ^{d/} 17.0 = 1.2 ^{d/} 14.7 = 0.9
Protoporphyrin, ug/100 ml RBC	23.1 = 1.0	21.7 = 1.1	27.7 = 3.3
Urine			
Coproporphyrin, ug/24 hr	10.7 = 5.9	1.1 = 0.6	4.9 = 2.4
ALA, ug/24 hr	97.4 = 19.2	101.4 = 30.1	50.5 = 6.6

^{a/} Number of rats per period, except where indicated otherwise.

^{b/} Mean ± standard error.

^{c/} Two rats.

^{d/} Six rats.

TABLE 17

TISSUE AND BODY FLUID CHEMISTRY OF RATS FED PAINT
FILM CONTAINING 2.0% LEAD AS LEAD OCTOATE

Analyses	Treatment Week		
	0 (N=4) ^{a/}	8 (N=4)	13 (N=12)
Serum electrophoresis			
Albumin, %	41 ± 3 ^{b/}	46 ± 2	48 ± 2
Alpha 1 globulin, %	27 ± 2	22 ± 1	20 ± 1
Alpha 2 globulin, %	4 ± 1	4 ± 1	6 ± 1
Beta globulin, %	20 ± 1	19 ± 1	21 ± 1
Gamma globulin, %	9 ± 1	9 ± 1	6 ± 1
Total protein, %	5.7 ± 0.1	6.0 ± 0.1	6.2 ± 0.1
Albumin/globulin ratio	0.70 ± 0.07	0.85 ± 0.07	0.96 ± 0.07
Erythrocytes			
ALAD, umol. PBC/ 100 ml RBC/hr	Males: 24.1 ± 4.0 ^{c/} Females: 18.7 ± 1.0 ^{c/} Total: 21.4 ± 2.3	12.1 ± 1.7 ^{e/} 11.3 ± 0.2 ^{e/} 11.7 ± 0.7	11.4 ± 0.6 ^{d/} 16.3 ± 3.9 ^{d/} 13.8 ± 2.0
Protoporphyrin, ug/100 ml RBC	29.5 ± 2.8	30.8 ± 2.5	24.0 ± 2.2
Urine			
Coproporphyrin, ug/24 hr	1.6 ± 0.6	3.0 ± 0.8	7.7 ± 2.9
ALA, ug/24 hr	80.7 ± 17.3	82.7 ± 10.6	64.5 ± 9.8

- ^{a/} Number of rats per period, except where indicated otherwise.
^{b/} Mean ± standard error.
^{c/} Two rats.
^{d/} Six rats.

TABLE 18

TISSUE AND BODY FLUID CHEMISTRY OF RATS FED PAINT
FILM CONTAINING 0.4% LEAD AS LEAD CHROMATE

Analyses	Treatment Week		
	4 (N=6) ^{a/}	8 (N=6)	13 (N=12)
Serum electrophoresis			
Albumin, %	42 ± 2 ^{b/}	44 = 2	47 = 1
Alpha 1 globulin, %	28 ± 1	20 ± 2	22 ± 1
Alpha 2 globulin, %	4 ± 1	4 ± 1	5 ± 1
Beta globulin, %	19 ± 1	19 ± 1	21 ± 1
Gamma globulin, %	8 ± 3	12 ± 2	6 ± 1
Total protein, %	5.8 ± 0.2	6.0 ± 0.2	6.1 ± 0.1
Albumin/globulin ratio	0.71 ± 0.06	0.80 ± 0.08	0.90 ± 0.03
Erythrocyte			
ALAD, μmol. PBC/	Males: 23.4 ± 3.5 ^{e/}	14.1 ± 0.6 ^{e/}	15.7 ± 1.5 ^{d/}
100 ml RBC/hr	Females: 13.4 ± 0.9 ^{e/}	17.4 ± 0.1 ^{e/}	16.5 ± 1.4 ^{d/}
	Total: 18.4 ± 3.3	15.7 ± 1.0	16.1 ± 1.0
Protoporphyrin, μg/100 ml RBC	27.3 ± 2.8	28.3 ± 0.6	27.9 ± 2.1
Urine			
Coproporphyrin, μg/24 hr	8.2 ± 6.7	1.5 ± 0.7	6.3 ± 2.2
ALA, μg/24 hr	69.3 ± 6.6	65.2 ± 17.4	85.3 ± 31.4

^{a/} Number of rats per period, except where indicated otherwise.

^{b/} Mean ± standard error.

^{c/} Two rats.

^{d/} Six rats.

TABLE 19

TISSUE AND BODY FLUID CHEMISTRY OF RATS FEED PAINT
PASTE CONTAINING 1.95% LEAD AS LEAD CHROMATE

Chato

Analyses	Treatment Week		
	4 (N=6) ^{a/}	8 (N=4)	13 (N=10)
Serum electrophoresis			
Albumin, %	41 ± 2 ^{b/}	45 ± 1	47 ± 2
Alpha 1 globulin, %	25 = 1	19 ± 1	19 = 2
Alpha 2 globulin, %	4 = 1	4 ± 1	5 = 1
Beta globulin, %	20 ± 1	20 ± 1	23 = 1
Gamma globulin, %	9 ± 1	11 ± 1	6 = 1
Total protein, %	5.7 ± 0.1	6.20 ± 0.04	6.4 ± 0.1
Albumin/globulin ratio	0.73 ± 0.06	0.81 ± 0.04	0.94 ± 0.08
Erythrocyte			
ALAD, μmol. PBC/ 100 ml RBC/hr	Males: 29.5 ± 3.1 ^{c/}	12.3 ± 1.0 ^{e/}	13.3 ± 1.4 ^{d/}
	Females: 20.4 ± 4.3 ^{c/}	14.7 ± 0.6 ^{e/}	12.9 ± 2.1 ^{d/}
	Total: 24.9 ± 3.4	13.5 ± 0.8	13.1 ± 1.3
Protoporphyrin, μg/100 ml RBC	26.5 ± 4.7	26.8 ± 1.8	27.4 ± 1.5
Urine			
Coproporphyrin, μg/24 hr	0.9 ± 0.1	7.0 = 6.6	4.4 = 1.9
ALA, μg/24 hr	80.8 ± 7.2	67.7 = 6.8	66.5 = 17.5

- ^{a/} Number of rats per period, except where indicated otherwise.
^{b/} Mean ± standard error.
^{c/} Two rats.
^{d/} Six rats.

TABLE 20

TISSUE AND BODY FLUID CHEMISTRY OF RATS FED DIET
CONTAINING 10,000 PPM LEAD AS LEAD DIBROMIDE

Analyses	Treatment Week		
	4 (N=4) ^a	8 (N=4)	13 (N=4)
Serum electrophoresis			
Albumin, %	40 = 2 ^b	47 = 3	46 = 2
Alpha 1 globulin, %	27 = 1	21 = 1	21 = 1
Alpha 2 globulin, %	3 = 1	4 = 1	5 = 1
Beta globulin, %	22 = 1	18 = 1	22 = 1
Gamma globulin, %	8 = 1	9 = 2	6 = 1
Total protein, mg %	5.6 = 0.1	5.1 = 0.1	6.4 = 0.1
Albumin/globulin ratio	0.68 = 0.05	0.90 = 0.12	0.88 = 0.06
Erythrocyte			
ALAD, μ mol. PBG/	Males: 26.4 = 7.4 ^{E/}	16.5 = 1.4 ^{E/}	12.6 = 1.6 ^{u/}
100 ml RBC/hr	Females: 14.3 = 3.2 ^{E/}	13.4 = 3.8 ^{E/}	13.7 = 1.1 ^{u/}
	Total: 20.3 = 4.9	15.0 = 1.9	13.1 = 1.0
Protoporphyrin,	25.5 = 1.6	24.2 = 2.6	24.6 = 2.0
ug/100 ml RBC			
Urine			
Coproporphyrin,	2.6 = 1.8	0.9 = 0.1	2.6 = 0.9
ug/24 hr			
ALA,	89.7 = 19.3	78.4 = 6.8	49.7 = 12.5
ug/24 hr			

^a Number of rats per period, except where indicated otherwise.

^b Mean = standard error.

^{E/} Two rats.

^{u/} Six rats.

TABLE 21

TISSUE AND BODY FLUID CHEMISTRY OF RATS FED PAIN
PAIN CONTAINING 56.05% LEAD AS LEAD CARBONATE

Analyses	Treatment Group		
	4 (N=3) ^a	8 (N=4)	13 (N=3)
Serum electrophoresis			
Albumin, %	41 = 6	45 = 1	47 = 2
Alpha 1 globulin, %	27 = 1	21 = 2	22 = 1
Alpha 2 globulin, %	3 = 1	4 = 1	5 = 1
Beta globulin, %	21 = 2	19 = 1	20 = 1
Gamma globulin, %	8 = 2	10 = 1	7 = 1
Total protein, %	5.4 = 0.2	6.0 = 0.06	6.3 = 0.1
Albumin/globulin ratio	0.73 = 0.17	0.82 = 0.04	0.56 = 0.06
Erythrocyte			
ALAD, nmol. PBC/			
100 ml RBC/hr	Males: 12.15 ^b	4.4 = 0.1 ^d	5.4 = 1.0 ^e
	Females: 9.1 = 2.1 ^d	12.4 = 0.4 ^d	7.4 = 0.8 ^e
	10.2 = 1.6 ^f	8.4 = 2.3 ^f	6.4 = 0.7 ^f
Protoporphyrin, ug/100 ml RBC	23.2 = 0.9	20.4 = 2.1	27.2 = 6.8
Urine			
Coproporphyrin, ug/24 hr	2.0 = 0.7	0.8 = 0.3	6.7 = 2.2
ALA, ug/24 hr	90.3 = 27.7	72.3 = 13.4	42.2 = 3.8

- a/ Number of rats per period, except where indicated otherwise.
 b/ Mean ± standard error.
 c/ One rat.
 d/ Two rats.
 e/ Six rats.
 f/ Significantly different from control (P < 0.05) as shown by Dunnett's multiple-comparison test following an analysis of variance.

TABLE 22

TISSUE AND BODY FLUID CHEMISTRY OF RATS FED VES
LEAD PAINT CONTAINING 11.0% LEAD

Analysis	Treatment Week		
	4 (N=12) ^a	8 (N=6)	13 (N=12)
Serum electrophoresis			
Albumin, %	52 = 1 ^b / ₂	44 = 1	44 = 1
Alpha 1 globulin, %	21 = 1	21 = 2	24 = 1
Alpha 2 globulin, %	4 = 1	8 = 3	7 = 1
Beta globulin, %	20 = 1	21 = 3	21 = 1
Gamma globulin, %	3 = 1	6 = 1	5 = 1
Total protein, %	5.4 = 0.2	6.0 = 0.2	6.1 = 0.1
Albumin/globulin ratio	1.1 = 0.03	0.78 = 0.06	0.82 = 0.06
Erythrocyte			
ALAD, umol. PBG/ 100 ml RBC/hr	Males: 8.5 = 5.0 ^c / ₂ Females: 10.1 = 0.1 ^d / ₂ Total: 9.3 = 2.1 ^d / ₂	5.0 = 0.3 ^e / ₂ 15.0 = 5.1 ^e / ₂ 10.0 = 3.6	4.9 = 0.6 ^d / ₂ 8.8 = 1.0 ^d / ₂ 6.9 = 0.6 ^e / ₂
Protoporphyrin, ug/100 ml RBC	14.8 = 4.3	24.5 = 1.8	28.3 = 1.2
Urine (N=4)			
Coproporphyrin, ug/24 hr	2.0 = 0.8	6.8 = 4.9	4.6 = 2.1
ALA, ug/24 hr	110.2 = 21.5	72.0 = 13.6	51.3 = 3.6

a/ Number of rats per period, except where indicated otherwise.

b/ Mean = standard error.

c/ Two rats.

d/ Six rats.

e/ Significantly different from control (P < 0.05) as indicated by Dunnett's multiple-comparison test following an analysis of variance.

TABLE 2)
SUMMARY OF PORPHYRIN METABOLISM IN RATS FED PAINT FOR 13 WEEKS
CONTAINING DIFFERENT CONCENTRATIONS OF LEAD

Diet	N ^{c/}	Erythrocyte		Urinary	
		ALA ^{a/} (μ mol. PPG/100 ml RBC/hr)	Protoporphyrin (μ g/100 ml RBC)	Coproporphyrin (μ g/25 hr)	(μ g)
Control	24	15.0 \pm 1.0 ^{d/}	29.2 \pm 2.0	6.0 \pm 1.9	43.
0.08% Lead Octoate	12	14.0 \pm 1.4	22.8 \pm 2.5	2.9 \pm 1.4	35.
0.53% Lead Octoate	12	14.7 \pm 0.9	27.7 \pm 3.3	4.9 \pm 2.4	50.
2.05% Lead Octoate	12	13.8 \pm 2.0	24.0 \pm 2.2	7.7 \pm 2.9	64.
0.42% Lead Chromate	12	16.1 \pm 1.0	27.9 \pm 2.1	6.3 \pm 2.2	85.
1.95% Lead Chromate	12	13.1 \pm 1.3	27.4 \pm 1.5	4.4 \pm 1.9	66.
12.43% Lead Chromate	12	13.1 \pm 1.0	24.6 \pm 2.0	2.6 \pm 0.8	49.
66.05% Lead Chromate	12	6.4 \pm 0.7 ^{e/}	27.2 \pm 6.8	6.7 \pm 1.2	42.
11.92% NBS Lead Paint	12	6.9 \pm 0.8 ^{e/}	26.3 \pm 1.2	4.6 \pm 2.1	51.

a/ δ -Aminolevulinic acid dehydrase.

b/ δ -Aminolevulinic acid.

c/ Number of rats per diet.

d/ Average \pm standard error of number of rats indicated.

e/ Significantly different from control ($P < 0.05$) as shown by Dunnett's Multiple-comparison test in analysis of variance.

0007-SWP-037009

0007-SWP-000115577

By 13 weeks the sex difference had disappeared and the ALAD activity in 66.05% lead carbonate group and the 11.92% NBS lead paint group were depressed 56% and 51%, respectively.

Urinalysis of rats fed paint ^{chips} containing different concentrations of lead are shown in Table 24-32. No marked differences in urinary protein or sediment (erythrocyte, crystals, casts, etc.). Thus, urinalysis can be considered within normal ranges for all treatment groups.

H. Lead Content in Tissues of Rats Fed Paint ^{chips} Containing Different Concentrations of Lead

^{change} Tables 33-37 show the lead content of blood, brain, liver, kidney, and bone from rats fed paint ^{chips} containing ^{paint chips containing} different concentrations of lead. The values for the lead concentrations in blood at 4 and 8 weeks were omitted from Table 23 because it was discovered that these samples had been contaminated by their storage containers. At 13 weeks the blood lead levels in the rats fed lead octoate and the rats fed 0.42% and 1.95% lead carbonate were not different from control. In the rats fed 12.43% lead chromate, 66.05% lead carbonate, ^{11.92% NBS lead paint}, blood levels were found to be elevated significantly. ^(p.01 M-T/gm)

^{lead in} At 4 weeks, tissue lead levels in brain, liver and kidney were below the detection limits of our assay. The results were the same at 8 weeks with the exception of the NBS lead paint group. All four rats in this group showed detectable lead in their kidneys.

At 13 weeks, detectable levels of lead in the brain appeared only in the rats fed 11.92% NBS lead paint. ^{Paint chips} In the liver detectable levels of lead were found in two rats fed 66.05% lead carbonate and nine rats fed 11.92% NBS lead paint. No lead was detected in the kidneys of the control group at 13 weeks. In contrast, lead was detected in the kidneys of one (two rats in each lead octoate group) and the 0.42% and 1.95% lead chromate groups. Lead was detected in the kidneys of three rats, eight rats and 12 rats in the 12.43% lead chromate, 66.05% lead carbonate and 11.95% NBS lead paint groups, respectively.

² The femurs of rats fed the control diet, lead octoate or lead chromate exhibited very little lead at 4 weeks. However, the femurs of rats fed 66.05% lead carbonate or 11.92% NBS lead paint contained 13.0 and 1.9 μ g of lead/gm of bone, respectively.

TABLE 24

URINALYSIS OF RATS FED PAINT ^{change} CONTAINING VC 1250

	Treatment Week		
	4	8	13
Protein: Negative	7	6	20
< 100 mg %	1	2	4
> 100 mg %			

Microscopic Examination			
RBC ^{a/} : Normal	7	5	23
Moderate	1	2	1
Excessive		1	
WBC ^{b/} : Normal	6	7	21
Moderate	2		2
Excessive		2	1
Epithelium ^{c/} : Normal	8	8	14
Moderate			
Excessive			
Crystals ^{c/} : Normal	4	8	23
Moderate	2		
Excessive	2		
Casts: Negative	8	8	24
Positive			

Numbers indicate number of rats at response level.

- a/ Normal, 10 or less cells; moderate, 10-100 cells; excessive, > 100 cells/field (x 450).
- b/ Normal, 5 or less cells; moderate, 5-25 cells; excessive, > 25 cells/field (x 100).
- c/ Normal, none; moderate, 1-5 crystals; excessive, > 5 crystals/field (x 100).

TABLE 25

**URINALYSIS OF RATS FED PAINT ⁴⁰⁰⁰ CONTAINING
0.07% LEAD AS LEAD OCTOATE**

	Treatment Week		
	4	8	13
Protein: Negative	4	3	8
< 100 mg %			
> 100 mg %		1	

Microscopic Examination			
RBC ^a : Normal	4	3	10
Moderate		1	2
Excessive			

WBC ^b : Normal	3	3	10
Moderate	2	1	2
Excessive			

Epithelium ^c : Normal	3	4	12
Moderate			
Excessive			

Crystals ^c : Normal	2	4	11
Moderate	2		1
Excessive			

Casts: Negative	4	4	12
Positive			

Numbers indicate number of rats at response level.

- a/ Normal, 10 or less cells; moderate, 10-100 cells; excessive, > 100 cells/field (x 400).
- b/ Normal, 5 or less cells; moderate, 5-25 cells; excessive, > 25 cells/field (x 100).
- c/ Normal, none; moderate, 1-5 crystals; excessive, > 5 crystals/field (x 100).

TABLE 26

chips
URINALYSIS OF RATS FED PAINT FILM CONTAINING
0.53% LEAD AS LEAD OCTOATE

	Treatment Week		
	4	8	13
Protein: Negative	4	3	10
< 100 mg %		1	1
> 100 mg %			1

Microscopic Examination			
RBC ^{a/} : Normal	2	2	10
Moderate	1	2	1
Excessive	1		1

WBC ^{b/} : Normal	4	1	9
Moderate		3	3
Excessive			

Epithelium ^{c/} : Normal	4	4	12
Moderate			
Excessive			

Crystals ^{c/} : Normal	3	4	12
Moderate	1		
Excessive			

Casts: Negative	4	4	12
Positive			

Numbers indicate number of rats at response level.

- a/ Normal, 10 or less cells; moderate, 10-100 cells; excessive, > 100 cells/field (x 440).
 b/ Normal, 5 or less cells; moderate, 5-25 cells; excessive, > 25 cells/field (x 100).
 c/ Normal, none; moderate, 1-5 crystals; excessive, > 5 crystals/field (x 100).

TABLE 27

China
URINALYSIS OF RATS FED PAINT ~~FROM~~ CONTAINING
2.05% LEAD AS LEAD OCTOATE

	Treatment Week		
	4	8	13
Protein: Negative	4	4	11
< 100 mg %			1
> 100 mg %			

Microscopic Examination			
RBC ^{a/} : Normal	4	4	12
Moderate			
Excessive			

WBC ^{b/} : Normal	3	3	8
Moderate	1		4
Excessive		1	

Epithelium ^{c/} : Normal	4	4	12
Moderate			
Excessive			

Crystals ^{d/} : Normal	2	4	12
Moderate			
Excessive	2		

Casts: Negative	4	4	12
Positive			

Numbers indicate number of rats at response level.

- a/ Normal, 10 or less cells; moderate, 10-100 cells; excessive, > 100 cells/field (x 440).
 b/ Normal, 5 or less cells; moderate, 5-25 cells; excessive, > 25 cells/field (x 100).
 c/ Normal, none; moderate, 1-5 crystals; excessive, > 5 crystals/field (x 100).

TABLE 28

chip
URINALYSIS OF RATS FED PAINT CONTAINING
0.2% LEAD AS LEAD CHROMATE

	Treatment Week		
	4	8	12
Protein: Negative	4	2	10
< 100 mg %		2	1
> 100 mg %			1

Microscopic Examination			
WBC ^a : Normal	3	1	8
Moderate	1	3	3
Excessive			1

WBC ^b : Normal	2	3	8
Moderate	2	1	1
Excessive			3

Epithelium ^c : Normal	4	4	12
Moderate			
Excessive			

Crystals ^d : Normal	2	4	12
Moderate	1		
Excessive	1		

Casts: Negative	4	4	12
Positive			

Numbers indicate number of rats at response level.

- a/ Normal, 10 or less cells; moderate, 10-100 cells; excessive, > 100 cells/field (x 40).
 b/ Normal, 5 or less cells; moderate, 5-25 cells; excessive, > 25 cells/field (x 100).
 c/ Normal, none; moderate, 1-5 crystals; excessive, > 5 crystals/field (x 100).

TABLE 29

(chip)
URINALYSIS OF RATS FED PAINT FILM CONTAINING
1.95% LEAD AS LEAD CHROMATE

	Treatment Week		
	4	8	12
Protein: Negative	3	3	11
< 100 mg %	1		1
> 100 mg %		1	

Microscopic Examination			
RBC ^a /: Normal	4	3	12
Moderate		1	
Excessive			

WBC ^b /: Normal	2	3	8
Moderate	2		1
Excessive		1	

Epithelium ^c /: Normal	4	4	12
Moderate			
Excessive			

Crystals ^e /: Normal	4	4	12
Moderate			
Excessive			

Casts: Negative	4	4	12
Positive			

Numbers indicate number of rats at response level.

a/ Normal, 10 or less cells; moderate, 10-100 cells; excessive, > 100 cells/field (x 440).

b/ Normal, 5 or less cells; moderate, 5-25 cells; excessive, > 25 cells/field (x 100).

c/ Normal, none; moderate, 1-5 crystals; excessive, > 5 crystals/field (x 100).

TABLE 30

chip¹
URINALYSIS OF RATS FED PAINT PASTE CONTAINING
12.5% LEAD AS LEAD CHROMATE

	Treatment Week		
	1	8	13
Protein: Negative	1	1	9
< 100 mg %	3	2	3
> 100 mg %		1	

Macroscopic Examination			
RBC ^{a/} : Normal	4	1	11
Moderate			1
Excessive		3	

WBC ^{a/} : Normal	1	1	11
Moderate	3	1	
Excessive		2	1

Epithelium ^{b/} : Normal	4	4	11
Moderate			1
Excessive			

Crystals ^{c/} : Normal	2	4	12
Moderate	2		
Excessive			

Casts: Negative	4	4	12
Positive			

Numbers indicate number of rats at response level.

- a/ Normal, 10 or less cells; moderate, 10-100 cells; excessive, > 100 cells/field (x 400).
- b/ Normal, 5 or less cells; moderate, 5-25 cells; excessive, > 25 cells/field (x 100).
- c/ Normal, none; moderate, 1-5 crystals; excessive, > 5 crystals/field (x 100).

TABLE 31

URINALYSIS OF RATS FED PAINT ^{chip} CONTAINING
65.35% LEAD AS LEAD CARBONATE

	Treatment Week		
	1	2	13
Protein: Negative	3	4	11
< 100 mg %	1		1
≥ 100 mg %			

Microscopic Examination			
RBC ^a /: Normal	4	2	11
Moderate		2	1
Excessive			

WBC ^b /: Normal	2	2	10
Moderate	2	2	2
Excessive			

Epithelium ^c /: Normal	4	4	12
Moderate			
Excessive			

Crystals ^c /: Normal	3	4	12
Moderate			
Excessive	1		

Casts: Negative	4	4	12
Positive			

Numbers indicate number of rats at response level.

a/ Normal, 10 or less cells; moderate, 10-100 cells; excessive, > 100 cells/field (x 440).

b/ Normal, 5 or less cells; moderate, 5-25 cells; excessive, > 25 cells/field (x 100).

c/ Normal, none; moderate, 1-5 crystals; excessive, > 5 crystals/field (x 100).

TABLE 32

URINALYSIS OF RATS FED PAINT ^{chip} CONTAINING
 11.9% LEAD (MPS LEAD PAINT)

	Treatment Week		
	2	3	13
Protein: Negative	2	3	7
< 100 mg %	2		5
> 100 mg %		1	

Microscopic Examination			
RBCs ^a : Normal	2	4	12
Moderate	2		
Excessive			

WBCs ^b : Normal	2	3	11
Moderate		1	1
Excessive	2		

Epithelium ^c : Normal	2	4	12
Moderate			
Excessive			

Crystals ^d : Normal	4	4	12
Moderate			
Excessive			

Casts: Negative	2	4	12
Positive			

Numbers indicate number of rats at response level.

- a/ Normal, 10 or less cells; moderate, 10-100 cells; excessive, > 100 cells/field (x 440).
- b/ Normal, 5 or less cells; moderate, 3-25 cells; excessive, > 25 cells/field (x 100).
- c/ Normal, none; moderate, 1-5 crystals; excessive, > 5 crystals/field (x 100).

TABLE 33

LEAD CONTENT OF WHOLE BLOOD

Diet	Treatment Week		
	<u>1^a</u>	<u>5^a</u>	<u>13^b</u> (8) <u>c</u>
Control ^d			13.1 = 0.9 (16) ^e
0.03% Lead Octoate			12.8 = 0.8 (8)
0.53% Lead Octoate			16.4 = 2.4 (7) ^f
2.05% Lead Octoate			14.5 = 1.5 (8)
0.42% Lead Chromate			13.2 = 1.0 (8)
1.95% Lead Chromate			12.0 = 1.4 (8)
12.43% Lead Chromate			19.4 = 1.2 (8) ^g
66.05% Lead Carbonate			24.9 = 2.2 (8) ^h
11.92% NBS Lead Paint			23.9 = 1.3 (12) ⁱ

^a/ Values deleted due to contamination.

^b/ Four values deleted due to contamination.

^c/ Number of rat bloods analyzed per group unless indicated otherwise.

^d/ Sixteen blood samples were analyzed.

^e/ Average μg of lead/100 ml blood = standard error of number of rats in parenthesis.

^f/ One blood sample lost.

^g/ Significantly different from control ($P < 0.05$) as shown by Dunnett's multiple-comparison test following an analysis of variance.

^h/ Twelve blood samples analyzed.

TABLE 34

LEAD CONTENT OF BRAIN

Diet	Treatment Week		
	<u>4</u> (4) ^{a/}	<u>8</u> (4)	<u>13</u> (12)
Control ^{b/}	n.d. ^{c/}	n.d.	n.d.
0.08% Lead Octoate	n.d.	n.d.	n.d.
0.53% Lead Octoate	n.d.	n.d.	n.d.
2.05% Lead Octoate	n.d.	n.d.	n.d.
0.42% Lead Chromate	n.d.	n.d.	n.d.
1.95% Lead Chromate	n.d.	n.d.	n.d.
12.43% Lead Chromate	n.d.	n.d.	n.d.
66.05% Lead Carbonate	n.d.	n.d.	n.d.
11.92% NBS Lead Paint	n.d.	n.d.	<u>0.2 ± 0.1^{d/}</u> (7)

^{a/} Number of brains analyzed per group unless indicated otherwise.

^{b/} Eight brains were analyzed at 4 and 8 weeks. Twenty-four brains were analyzed at 13 weeks.

^{c/} Not detectable. Below sensitivity of 0.07 µg/gm of brain.

^{d/} Average µg of lead/gm brain ± standard error number of rats shown in parenthesis.

TABLE 35

LEAD CONTENT OF LIVER

Diet	Treatment Week		
	\bar{x} (4) ^d	\bar{x} (8)	\bar{x} (13)
Control ^{b/}	n.d. ^{c/}	n.d.	n.d.
0.08% Lead Octoate	n.d.	n.d.	n.d.
0.53% Lead Octoate	n.d.	n.d.	n.d.
2.05% Lead Octoate	n.d.	n.d.	n.d.
0.42% Lead Chromate	n.d.	n.d.	n.d.
1.95% Lead Chromate	n.d.	n.d.	n.d.
12.43% Lead Chromate	n.d.	n.d.	n.d.
66.05% Lead Carbonate	n.d.	n.d.	$\frac{1.1}{0.4} = 0.6\bar{6}$ (2)
11.92% NBS Lead Paint	n.d.	n.d.	$\frac{0.4}{0.4} = 0.1$ (9)

^{a/} Number of livers analyzed per group unless indicated otherwise.

^{b/} Eight livers were analyzed at 4 and 8 weeks. Twenty-four livers were analyzed at 13 weeks.

^{c/} Not detectable. Below sensitivity of 0.07 ug/gm liver.

^{d/} Values are average ug of lead/gm liver ± standard error of number of rats shown in parenthesis.

TABLE 36

LEAD CONTENT OF KIDNEY

Dose	Treatment Week		
	0	4	8
	(n) ^{a/}	(n)	(n)
Control ^{b/}	n.d. ^{c/}	n.d.	n.d.
0.08% Lead Octoate	n.d.	n.d.	2.38 (2)
0.53% Lead Octoate	n.d.	n.d.	0.38 (1)
2.05% Lead Octoate	n.d.	n.d.	0.38 = 0.1 (2)
0.42% Lead Chromate	n.d.	n.d.	0.52 (1)
1.95% Lead Chromate	n.d.	n.d.	0.51 (1)
12.43% Lead Chromate	n.d.	n.d.	0.4 = 0.0 (3)
66.05% Lead Carbonate	n.d.	n.d.	2.3 = 0.2 (8)
11.92% NBS Lead Paint	n.d.	1.4 = 0.1 ^{b/} (4)	1.96 = 0.1 (12)

- a/ Number of kidneys analyzed per group unless otherwise indicated.
- b/ Eight kidneys were analyzed at 4 and 8 weeks. Twenty-four kidneys were analyzed at 13 weeks.
- c/ Not detectable. Below sensitivity of 0.07 ug/gm kidney.
- d/ Values are ug of lead/gm kidney or average ug of lead/gm kidney = standard error of number of rats in parenthesis.

where NBS.

See conclusion
X X X

Confirms
check
Table.

TABLE 37

LEAD CONTENT OF BONE (FEMUR)

Diet	Treatment Week		
	4 (4) ^{a/}	8 (4)	13 (12)
Control ^{b/}	1.6 ^{c/} (1)	3.9 ± 0.4 (8)	3.2 ± 0.2 (24)
0.08% Lead Octoate	3.1 (1)	4.2 ± 0.6 (4)	3.3 ± 0.3 (12)
0.53% Lead Octoate	n.d. ^{d/}	3.9 ± 0.2 (4)	3.1 ± 0.2 (12)
2.05% Lead Octoate	n.d.	3.0 ± 0.7 (4)	3.9 ± 0.5 (12)
0.42% Lead Chromate	2.9 (1)	2.6 ± 0.9 (4)	3.8 ± 0.6 (12)
1.95% Lead Chromate	0.9 (1)	1.8 ± 0.2 (4)	4.1 ± 0.5 (12)
12.43% Lead Chromate	3.3 (1)	3.1 ± 1.1 (4)	3.5 ± 0.5 (10)
66.05% Lead Carbonate	13.0 ± 4.1 (4)	16.0 ± 2.1 (4) ^{e/}	21.7 ± 2.4 (12) ^{e/}
11.92% NBS Lead Paint	14.9 ± 1.5 (4)	16.4 ± 0.4 (4) ^{e/}	10.9 ± 0.9 (12) ^{e/}

Lack of comment on chart

- a/ Number of bones analyzed per group unless indicated otherwise.
- b/ Eight bones were analyzed at 4 and 8 weeks. Twenty-four bones were analyzed at 13 weeks.
- c/ Values are ug of lead/gm bone or average ug of lead/gm bone ± standard error of number of rats in parenthesis.
- d/ Not detectable. Below sensitivity of 0.4 ug/gm of bone.
- e/ Significantly different from control (P < 0.5) as shown by Dunnett's multiple comparison test following an analysis of variance.

e - 2 samples lost.

? 0.05

At 8 weeks, the femurs of rats fed the control, lead octoate or lead chromate diets contained similar quantities of lead, ranging from 1.8-4.2 ug lead/gm bone. Lead content in the femurs in the 66.05% lead carbonate and 11.92% NBS groups were 10.0 and 10.9 ug lead/gm bone, respectively. Both of these values were significantly above control.

After 13 weeks, the rats fed lead octoate or lead chromate had no more lead in their femurs than at 8 weeks and these levels were no higher than those in the control group. The 66.05% lead carbonate group exhibited some higher levels of lead in their femurs (21.7 ug lead/gm bone) than at 8 weeks. The 11.92% NBS lead paint group had less lead in their femurs (10.9 ug lead/gm bone) than at 8 weeks. The lead levels in both of these groups were significantly greater than those observed in the control rats.

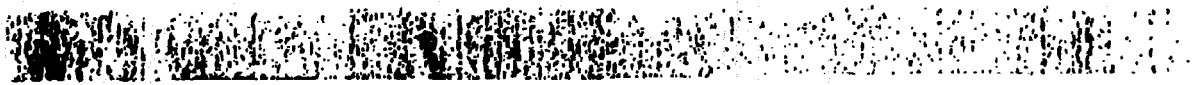
^{Chrys}
I. Pathology of Rats Fed Paints Containing Different Concentrations of Lead

The relative organ weights of the thyroid, spleen, heart, kidneys, liver, adrenals, brain and gonads are shown in Table 38. The Dunnett's multiple-comparison test showed that none of the relative organ weights differed from control values.

The pathology of rats fed the control, 2.05% lead octoate, 12.43% lead chromate, 66.05% lead carbonate or 11.92% NBS lead paint diets for 13 weeks is shown in Tables 39-43. ^(table) The control rats had a few naturally occurring lesions. Fourteen of these rats had mild to moderate lymphoid hyperplasia in the lungs, characteristic of early minute pneumonia. One of these rats had a moderate pneumonia and another one a mild emphysema.

^{Cont. P}
Other lesions included an unspecific myocarditis in two rats; foci of subacute inflammation in the liver of two rats; a cross-section of a parasite (roundworm) in the colon of one rat; and foci of mononuclear cell infiltration in the kidneys of two rats. The bone marrow myeloid/erythroid cell ratios (M/E) of all rats were within normal limits.

The lesions observed in rats fed the 2.05% lead octoate diet were similar to the lesions seen in the control rats. Seven out of the 12 rats ⁽⁸⁻⁸⁷⁶⁾ had mild to moderate lymphoid hyperplasia in the lungs and one had mild pneumonia. Four rats had mild ⁽⁸⁻⁸⁷⁶⁾ of subacute inflammation in the liver characterized by a loss of several hepatic cord cells which were replaced by macrophages and lymphocytes. Another rat had a focus of inflammation in the interstitial tissue of the pancreas. The M/E ratios of these rats were normal.



of Station - standard error of number that is indicated.

Station	Height	Distance	Angle	Area	Volume	Weight	Value	Standard Error
10	10.00	10.00	10.00	10.00	10.00	10.00	10.00	10.00
11	11.00	11.00	11.00	11.00	11.00	11.00	11.00	11.00
12	12.00	12.00	12.00	12.00	12.00	12.00	12.00	12.00
13	13.00	13.00	13.00	13.00	13.00	13.00	13.00	13.00
14	14.00	14.00	14.00	14.00	14.00	14.00	14.00	14.00
15	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00
16	16.00	16.00	16.00	16.00	16.00	16.00	16.00	16.00
17	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00
18	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00
19	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00
20	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00
21	21.00	21.00	21.00	21.00	21.00	21.00	21.00	21.00
22	22.00	22.00	22.00	22.00	22.00	22.00	22.00	22.00
23	23.00	23.00	23.00	23.00	23.00	23.00	23.00	23.00
24	24.00	24.00	24.00	24.00	24.00	24.00	24.00	24.00
25	25.00	25.00	25.00	25.00	25.00	25.00	25.00	25.00
26	26.00	26.00	26.00	26.00	26.00	26.00	26.00	26.00
27	27.00	27.00	27.00	27.00	27.00	27.00	27.00	27.00
28	28.00	28.00	28.00	28.00	28.00	28.00	28.00	28.00
29	29.00	29.00	29.00	29.00	29.00	29.00	29.00	29.00
30	30.00	30.00	30.00	30.00	30.00	30.00	30.00	30.00

TABLE 10
STATION DATA FOR THE SURVEY

TABLE 40
 PATHOLOGY OF RATS FED FOR 13 WEEKS WITH PAINT FILM CONTAINING
 2.05% LEAD AS LEAD OXIDATE

	83	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
<u>Lungs</u>																
Lymphoid hyperplasia					1 ²	2	1	1	1	1	1	1	1	1	2	1
Pneumonia					1											
<u>Liver</u>																
Foci of inflammation	1			1									1			1
<u>Pancreas</u>																
Foci of inflammation																
<u>Bone Marrow</u>																
M/F ratio	1.2	1.0	1.7	1.0	1.2	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.4	1.2	1.3	1.8

Lesions not listed were normal.

2/ Severity of lesions: 1-minimal; 2-moderate; 3-severe; 4-very severe; ± questionable

TABLE 41

PATHOLOGY OF RATS FED FOR 13 WEEKS WITH PAINT FILM CONTAINING
12.5% LEAD AS LEAD CHROMATE

	143	146	147	148	149	150	153	156	157	158	159	160
<u>Lungs</u>												
Lymphoid hyperplasia	2 ^{a/}	2		1		1				2	2	1
Pneumonia	1											
<u>Heart</u>												
Myocarditis												
<u>Bone Marrow</u>												
M/E ratio	1.2	1.0	1.0	1.2	1.1	1.4	1.1	1.4	1.5	1.4	1.2	1.5

Tissues not listed were normal.

a/ Severity of lesions: 1-minimal; 2-moderate; 3-severe; 4-very severe; † questionable.

TABLE 62

VALIQUANRY OF RATS FED FOR 13 WEEKS WITH PAINT FILM
CONTAINING 66.05% LEAD AS LEAD CARBONATE

Rat No.	162	166	167	168	169	170	173	176	177	178	179	180
<u>Lungs</u>												
Lymphoid hyperplasia		1 ^{a/}	1	1	1	1	1	2	2	1	1	1
Pneumonia						1						
<u>Heart</u>												
Myocarditis		1	2		1							
<u>Liver</u>												
Foci of inflammation	1											
<u>Skeletal muscle</u>												
Necrosis												
<u>Bone marrow</u>												
M/E ratio	1.2	1.2	1.2	1.0	1.1	1.3	1.2	1.0	1.4	1.3	1.1	1.4

Tissues not listed were normal.

a/ Severity of lesions: 1-minimal; 2-moderate; 3-severe; 4-very severe; 5-questionable

TABLE 43

PATHOLOGY OF RATS FED FOR 13 WEEKS WITH NBS LEAD PAINT
CONTAINING 11.9% LEAD

<u>Rat No.</u>	<u>183</u>	<u>184</u>	<u>185</u>	<u>186</u>	<u>189</u>	<u>190</u>	<u>193</u>	<u>194</u>	<u>195</u>	<u>196</u>
<u>Lungs</u>										
Lymphoid hyperplasia	2 ^{a/}	2		2		2			1	2
Pneumonia				2						
<u>Heart</u>										
Myocarditis			2		1					
<u>Liver</u>										
Foci of inflammation									1	
<u>Bone Marrow</u>										
H/E ratio	1.2	1.4	1.3	1.2	1.5	1.2	1.2	1.4	1.5	1.3

Tissues not listed were normal.

a/ Severity of lesions: 1-minimal; 2-moderate; 3-severe; 4-very severe; ± question

57

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(58.3%)
The rats fed the 12.43% lead chromate diet had lesions similar to the lesions seen in the control rats. Seven of 12 rats had mild to moderate lymphoid hyperplasia, and one had mild pneumonia. Only one rat had a moderate unspecific myocarditis. The M/E ratios were normal.

The lesions seen in the rats fed the 11.92% NBS lead paint diet were similar to those lesions seen in the control rats. Eight of 12 rats (66.7%) had different degrees of lymphoid hyperplasia in the lungs. In one rat pneumonia was evident. Unspecific myocarditis occurred in 2 rats while foci of inflammation in the liver were observed in only one rat. The M/E ratios were normal.

In conclusion, the pathology seen in the control and treated rats were characteristic of those in a normal population of rats. No evidence of lead-induced lesions were found.

IV. DISCUSSION

The levels of lead fed to rats in the study were sufficient to produce significant elevation of body lead burden if the lead is in the form of lead nitrate.^{13/} If we equate the amount of lead consumed by the average rat fed the 2.05% lead octoate, 12.43% lead chromate, 66.05% lead carbonate, and 11.92% NBS lead paint diets to a 14.6 kg (3-year old) child, we find that the lead consumption would equal 28.6, 123.7, 503.0 and 113.9 mg of lead/day, respectively. On the basis of a 2% lead paint, the total paint intake would be 1.5, 6.2, 25.0, and 5.7 gm/day. Daily ingestion of these quantities of old paint have been reported to produce lead poisoning.^{13/} ?

There were no changes in hematology, urinalysis or serum proteins throughout the entire study. However, there was one effect on porphyrin metabolism. As early as 4 weeks, rats fed either the 66.05% lead carbonate diet or the 11.92% NBS lead paint diet exhibited 50% depression of erythrocyte ALAD activity. This effect appeared to be directly related to the concentration of blood lead as has been reported by others.^{14,15/} However, there was one exception, blood lead in the 12.43% lead chromate group became elevated by the 13th week, but there was no depression of ALAD activity. This discrepancy could be related to the duration of elevated blood lead or the age of the animal when blood lead becomes elevated.

Even though erythrocyte ALAD was depressed 50%, the overall effect on porphyrin metabolism must be considered mild, since there was no concomitant change in the levels of protoporphyrin (erythrocyte), delta-aminolevulinic acid and coproporphyrin. These observations are consistent with reports that blood lead levels greater than 40 µg/100 ml RBC are needed before serious changes in porphyrin metabolism occur.^{15/}

The body lead burden of rats fed paint containing lead octoate or lead chromate were no different from control until 13 weeks. At this time lead was found in the kidneys of one to three rats on each of the lead octoate and lead chromate diets, and the blood lead levels in the 12.43% lead chromate group were significantly elevated. Since rats fed lead nitrate show elevated lead levels in blood, kidneys, bone and liver within 2 weeks, it appears that the lead octoate and lead chromate were not either readily absorbed or available for absorption.

Pathology was performed only on the rats that were fed the control, 2.05% lead octoate, 12.43% lead chromate, and 11.92% NRS lead paint diets for 13 weeks. All of these rats were relatively free of lesions, and those lesions which were observed, occur naturally in rat colonies.

V. CONCLUSIONS *planned*

newly made old type
This study shows that rats fed 0.1% diet (paint/feed) of old paint containing 11.92% lead and new paint containing 66.05% lead as lead carbonate exhibited early signs of lead poisoning. These signs consisted of erythrocyte ALAD depression (50%) and significant increases in blood, kidney, bone, liver and/or brain lead. Rats fed a diet consisting of 0.1% new paint film containing 12.43% lead as lead chromate exhibited only elevated blood lead after 13 weeks of feeding. A similar diet of new paint containing 2.05% lead as lead octoate produced no signs of lead poisoning.

The lack of any marked change in the body lead burden in these rats suggests that very little lead was absorbed from the gastrointestinal tract. Since there is considerable evidence that the rat can absorb lead in several forms, one must conclude that the lead in the paint used in this experiment was not readily available for absorption. In conclusion, the results reported herein support the contention that lead is not readily absorbed from the newer paints.

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*Lancet**

NEW CONCLUSION

Older paint formulations contained soluble lead salts. Two samples of paint chips representative of these formulations were fed to rats at 0.1% of their diets. One was supplied by the National Bureau of Standards and was removed from interior walls of older homes. It contained 11.92% lead. The other was a ~~lead~~ formulation containing 66.05% lead carbonate. Both of these samples produced classical signs of lead poisoning in the rats. These signs consisted of erythrocyte ALAD depression (50%) and significant increases in blood, kidney, bone, liver and/or brain lead.

Newer paint formulations contain insoluble lead pigments and low levels of lead driers. Several samples of paint chips containing up to 12.43% lead chromate pigment and up to 2.0% lead octoate drier were also fed to rats at 0.1% of their diets. The only evidence of toxicity or effect on body burden appear in the rats fed the paint containing 12.43% lead chromate. This consisted of an increase in blood lead, without other signs of poisoning. Paint containing 1.95% lead chromate and paint containing 2.05% lead octoate produced no detectable changes in the rats.

These studies show a marked difference in the toxicity of lead in paint formulations depending on the nature of the salt form and its solubility. The lack of toxicity with paints containing 2.0% lead chromate or lead octoate undoubtedly is due to the lack of significant absorption from the gastrointestinal tract.

Metric

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MODIFICATION OF CASTLES' DISCUSSION

The levels of lead fed to rats in the study were sufficient to produce significant elevation of body lead burden if the lead is in the form of lead nitrate.^{13/} If we equate the amount of lead consumed by the average rat fed paint chips containing 2.05% lead octoate, 12.45% lead chromate, 66.05% lead carbonate, and 11.92% NBS lead paint diets to a 14.6 kg (3-year old) child, we find that the lead consumption would equal 28.6, 125.7, 503.0 and 113.9 mg of lead/day, respectively. On the basis of a 2% lead paint, the total paint intake would be 1.5, 6.2, 25.0, and 5.7 gm/day *respectively*. Daily ingestion of these quantities of old paint have been reported to produce lead poisoning.^{13/}

containing white lead.

There were no changes in hematology, urinalysis or serum proteins throughout the entire study. ~~However~~, porphyrin metabolism was ~~affected~~ *affected* ~~as~~ *as* early as 4 weeks in rats fed either the 66.05% lead carbonate diet or the 11.92% NBS lead paint diet as evidenced in a 50% depression of erythrocyte ALAD activity. This effect appeared to be directly related to the concentration of blood lead as has been reported by others.^{14,15/} ~~However~~ there was one exception; blood lead in the 12.45% lead chromate group became elevated by the 13th week, but there was no depression of ALAD activity. This discrepancy could be related to the duration of elevated blood lead or the age of the animal when blood lead became elevated.

Even though erythrocyte ALAD was depressed 50%, the overall effect on porphyrin metabolism must be considered mild, since there was no concomitant change in the levels of protoporphyrin (erythrocyte), delta-aminolevulinic acid and coproporphyrin. These observations are consistent with reports that blood lead levels greater than 40 ug/100 ml RBC are needed before ~~serious~~ *serious* changes in porphyrin metabolism occur.^{14/}

The body lead burden of rats fed paint containing lead octoate or lead chromate ~~was~~ *was* no different from control until 13 weeks. At this time lead was found in the kidneys of one to three rats on each of the lead octoate and lead chromate diets, and the blood lead levels in the 12.45% lead chromate group were significantly elevated. Since rats fed lead nitrate show elevated lead levels in blood, kidneys, bone and liver within 2 weeks,^{15/} it appears that the lead octoate and lead chromate were ~~not~~ *not* either readily absorbed or ~~available~~ *available* for absorption.

Complete gross and microscopic pathology was performed on the rats that were fed the control, 2.05% lead octoate, 12.45% lead chromate, and 11.92% NBS lead paint diets for 13 weeks. All of these rats were relatively free of lesions, and those lesions which were observed, occur naturally in rat colonies.

No evidence that Pb paint included in the diets increased the formation of lesions.

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PREFACE

This report was prepared at Midwest Research Institute, 425 Volker Boulevard, Kansas City, Missouri 64110 under Contract No. 62-W-62GC & NPC, MRI Project No. 3729-B, "Lead Paint Ingestion Study." The Research was sponsored by the National Paint and Coatings Association, 1500 Rhode Island Avenue, N. W., Washington, D. C. 20005. Royal A. Brown, Technical Director, National Paint and Coatings Association was the project monitor.

The research was conducted in the Biological Sciences Division, under the direction of Dr. W. B. House from 1 December 1972 through 31 July 1973. Dr. Thomas R. Castles, Principal Pharmacologist, was the principal investigator, assisted by Dr. Jaime Sanyer, Associate Pathologist, and Mrs. Jane Hoch, Biology Research Assistant. Dr. James L. Spigarelli, Senior Chemist supervised the lead analysis with the assistance of Mrs. Hope M. Miller, Assistant Chemist.

Members of the National Paint and Coatings Association Industrial Metals Task Force prepared the paint chips and consulted with Drs. Castle, Sanyer, Spigarelli and House during the course of the study. The personnel of the NPCA Industrial Metals Task Force is as follows:

Richard A. Moore	-	The Sherwin Williams Company - Chairman
Royal A. Brown	-	The National Paint & Coatings Association
Dr. John P. Frawley	-	Hercules, Inc.
Charles M. Jackson	-	Celanese Coatings Co.
Joseph G. Kingston	-	Glidden-Durkee Division of SCM Corporation
Dr. Sidney Lauren	-	Coatings Research Group, Inc.
William W. Ringle	-	Pratt and Lambert, Inc.
Edwin E. Swain	-	E. I. duPont de Nemours & Co., Inc.
Jean P. Teas	-	The Flood Company
Domenic J. Tessari	-	De Soto, Inc.

Approved for:
MIDWEST RESEARCH INSTITUTE

W. B. House, Director
Biological Sciences Division

14 September, 1973

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SLIGHT MODIFICATION OF CASTLES' CONCLUSIONS

This study shows that rats fed 0.1% diet (paint/feed) of old paint containing 11.92% lead and new paint containing 66.05% lead as lead carbonate exhibited early signs of lead poisoning. These signs consisted of erythrocyte ALAD depression (50%) and significant increases in blood, kidney, bone, liver and/or brain lead. Rats fed a diet consisting of 0.1% new paint film containing 12.43% lead as lead chromate exhibited only elevated blood lead after 15 weeks of feeding. A similar diet of new paint containing 2.05% lead as lead octoate produced no signs of lead poisoning.

The lack of any marked change in the body lead burden in these lead chromate and lead octoate rats fed paint containing chromate and octoate suggests that very little lead was absorbed from the gastrointestinal tract. Since there is considerable evidence that the rat can absorb lead in several forms, one must conclude that the lead in the form of lead chromate and lead octoate and incorporated into paint was not readily available for absorption. In conclusion, the results reported herein support the contention that lead is not readily absorbed from the newer paints.

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