INTERNATIONAL LEAD ZINC RESEARCH ORGANIZATION, INC.

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July 30, 1970

To: All Members of the Environmental Health Committee

From: J. F. Cole, Sc. D.

Gentlemen:

Enclosed are two reports for your interest:

1) LH-151 Study Atmospheric Contaminants in Animals and Man
Three Month Progress Report - This report includes initial data on the exposure of rats and monkeys in preparation for the human volunteer study.

2) Toxicity of Orally - Administered Lead - Program Summary
This recently completed program was sponsored by the American Petroleum Institute at Hazelton Laboratories. Through the kind permission of Dr. H. H. Golz, Medical Director of the API, we are distributing copies to members of the ILZRO Environmental Health Committee. This report is for your personal use only. It should not be cited as a reference since it will be published in the near future by Hazelton and the API.

Sincerely,

Jerome F. Cole

J. F. Cole, Sc. D.
Manager, Environmental Health

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Enc.

LH151

July 13, 1970

INSTITUTE OF EXPERIMENTAL PATHOLOGY & TOXICOLOGY
ALBANY MEDICAL COLLEGE
ALBANY, NEW YORK

IN54 - LEAD
THREE-MONTH PROGRESS REPORT

Exposure of animals - rats and rhesus monkeys - to an atmosphere containing lead particulates was begun on March 12, 1970. In the experiment, the animals are exposed daily, 7 days a week, to lead sesquioxide particles at a nominal concentration of 20 μg per cubic meter. These particles are generated by burning tetraethyllead in propane.

Periodically, samples of chamber air, diet, water, blood, urine and feces have been obtained for estimation of lead content. Additionally, blood and urine samples have been subjected to certain routine clinical examinations and certain special tests which are indicative of lead intoxication.

The following is a brief discussion of the results obtained to date.

Chamber. The chamber is operated from 11:00 A.M. each morning until 9:00 A.M. the following morning. During the daily two-hour shut-down period, all necessary maintenance of the animals within the chamber is performed. Concentrations of atmospheric lead within the chamber are determined several times daily during the week and at least once each day on Saturday and Sunday. Measured volumes of air are withdrawn from the chamber through a filter having 0.2 micron sized pores. Material on the filter is then dissolved in dilute nitric acid and lead is estimated by atomic absorption spectrophotometry. The mean of the several determinations performed during each day is recorded as the lead concentration for that day. The average daily concentration of lead in the chamber during the first three months of operation was 20.2 ± μg per cubic meter.

Since the production of lead sesquioxide particles in the chamber has been by way of a heat generating process, careful monitoring of temperatures within the chamber has been performed. Both an industrial recording thermometer and a laboratory thermometer have been employed. The highest daily temperature observed has ranged from 79-86° F. The "usual" maximum is 81-82° F and during the 5 days that the temperature rose to 86°, there was a failure of the air conditioning system in the facility.

Lead in Blood. Periodic estimations of the lead content of blood have been performed on the animals in the chamber and the control animals. The results of these determinations are shown in Table 1. It is apparant that lead concentrations in both rats and monkeys are significantly greater in the animals housed in this chamber. Blood levels of rats in the chamber are nearly ten times the concentration of lead in the control animals. It is not yet possible to ascertain whether the levels are continually rising or whether they have reached a maximum, though fluctuating level.

It is also of interest to note the blood lead levels in the control animals. Levels in the monkeys have continually decreased since they were brought into the laboratory. In the control rats, however, which have always existed in a laboratory environment, the blood lead levels have maintained a constant low level.

Lead in Urine. Concentrations of lead found in urine are shown in Table 2. Although the trends are similar to those found in blood, the deviations are greater. This is partly a reflection of the wide variations between individual animals and partly due to the very low levels being estimated. The data are presented in a different form in Table 3. In this case the amount of lead excreted in the urine over a 24 hr period is shown. Here again is seen a trend toward higher amounts in the experimental animals.

Lead in Feces. Concentrations of lead in feces of the rats and monkeys is shown in Table 4. The excretion of fecal lead over a 24 hr period is shown in Table 5. Although the means are generally higher in the feces from animals exposed to lead in the chamber, the variations in results do not permit an unequivocal interpretation.

The lack of highly significant rises in urine and fecal lead in spite of the larger increase in blood lead levels may mean that some deposition of lead in tissues is occurring. This will be examined when samples of tissue are taken at autopsy for lead estimation.

Special Chemistry. Samples of urine have also been examined for levels of delta aminolevulinic acid, porphobilinogen and coproporphyrin-substances which are usually indicators of lead toxicity. In neither the rats nor the monkeys were there any differences between the experimental and control animals.

Clinical Chemistry and Hematology. Routine clinical and hematological examinations of blood have not revealed any differences between control and experimental animals. The parameters investigated were serum glucose, sodium, potassium, calcium, phosphorus and glutamic-pyruvic transaminase. No significant differences were noted in the hematological examinations.

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Project Leader

Cameron Russell
Alternate

KWA

Table 1. Concentration of Lead in Blood

	Time of determination	Control		Chamber	
		no. of animals	Pb conc. (μg/100 ml)	no. of animals	Pb conc. (μg/100 ml)
Monkeys	2 wk	4	7.8 ± 1.7	4	12.8 ± 1.3
	1 mo	4	5.0 ± 0.8	8	11.4 ± 1.3
	2 mo	4	4.3 ± 1.3	7	9.3 ± 2.3
	3 mo	4	3.3 ± 1.3	8	12.9 ± 3.1
Rats	1 mo	8	2.6 ± 0.5	8	12.8 ± 2.7
	2 mo	8	2.5 ± 0.8	8	9.8 ± 2.2
	3 mo	8	2.9 ± 0.4	7	26.6 ± 7.0

Table 2. Concentration of Lead in Urine

	Time of determination	Control		Chamber	
		no. of animals	Pb conc. (μg/100 ml)	no. of animals	Pb conc. (μg/100 ml)
Monkeys	0	-	-	7	3.1 ± 1.4
	2 wk	4	8.9 ± 3.3	8	9.4 ± 4.4
	1 mo	4	4.6 ± 1.2	8	4.8 ± 0.7
	2 mo	4	1.6 ± 0.8	8	4.9 ± 3.5
	3 mo	2	2.6 ± 1.7	8	6.0 ± 3.5
Rats	1 wk	8	2.5 ± 1.2	-	-
	1 mo	8	1.4 ± 1.0	6	3.2 ± 2.1
	2 mo	8	2.4 ± 2.4	8	3,5 ± 1.8
	4 mo	8	1.3 ± 0.2	8	5.7 ± 5.7

Table 3. Excretion of Lead in Urine

	Time of determination	Control		Chamber	
		no. of animals	Pb conc. (μg/24 hrs)	no. of animals	Pb conc. (μg/24 hrs)
Monkeys	0	-	-	7	9.2 ± 7.2
	2 wk	4	18.8 ± 17.8	8	13.4 ± 5.5
	1 mo	4	13.5 ± 8.7	8	9.6 ± 3.1
	2 mo	4	1.3 ± 0.7	8	12.3 ± 10.2
	3 mo	2	5.7 ± 4.9	8	10.3 ± 1.8
Rats	1 wk	8	0.30 ± 0.06	-	-
	1 mo	8	0.18 ± 0.07	6	0.32 ± 0.13
	2 mo	8	0.22 ± 0.08	8	0.44 ± 0.18
	3 mo	8	0.16 ± 0.03	8	0.49 ± 0.21

Table 4. Concentration of Lead in Feces

	Time of determination	Control		Chamber	
		no. of animals	Pb conc. (μg/g)	no. of animals	Pb conc. (μg/g)
Monkeys	0	-	-	7	2.7 ± 1.4
	2 wk	4	5.1 ± 2.3	8	3.4 ± 2.1
	1 mo	4	3.3 ± 0.6	8	6.1 ± 2.6
	2 mo	4	0.9 ± 0.7	8	4.6 ± 2.9
	3 mo	2	4.7 ± 3.5	6	8.1 ± 3.6
Rats	1 wk	8	4.4 ± 1.0	-	-
	1 mo	5	8.2 ± 6.9	7	8.6 ± 4.0
	2 mo	6	7.7 ± 6.4	7	10.1 ± 3.1
	3 mo	7	7.4 ± 7.3	4	5.3 ± 1.4

Table 5. Excretion of Lead in Feces

	Time of determination	Control		Chamber	
		no. of animals	Pb excreted (μg/24 hrs)	no. of animals	Pb excreted (μg/24 hrs)
Monkeys	0	-	-	7	12.1 ± 7.7
	2 wk	4	5.1 ± 2.3	8	21.1 ± 9.4
	1 mo	4	10.0 ± 4.8	8	12.1 ± 8.0
	2 mo	4	9.0 ± 5.5	8	4.8 ± 3.9
	3 mo	2	10.1 ± 4.1	6	13.0 ± 6.1
Rat	1 wk	8	4.6 ± 1.8	-	-
	1 mo	5	4.0 ± 2.3	7	6.0 ± 2.5
	2 mo	6	4.8 ± 2.3	7	6.3 ± 4.7
	3 mo	7	4.7 ± 2.5	4	5.3 ± 2.9