

PROPOSAL TO INTERNATIONAL LEAD ZINC ORGANIZATION FOR THE CONTINUATION, THROUGH THE YEAR 1971, OF THE FINANCIAL SUPPORT OF A PROGRAM OF RESEARCH, IN THE KETTERING LABORATORY, IN THE DEPARTMENT OF ENVIRONMENTAL HEALTH OF THE COLLEGE OF MEDICINE OF THE UNIVERSITY OF CINCINNATI, ON THE GENERAL SUBJECT OF "HUMAN EXPOSURE TO PARTICULATE LEAD COMPOUNDS IN THE AIR, UNDER EXPERIMENTAL CONDITIONS"

Subtitle Project LH 160 (Present Phase of Experimentation)  
Effect of Particle Size In Air on the Absorption of Lead by Man

The background of this investigation of the metabolism of lead in man, under a variety of conditions, over a period of years, will have been presented in prior proposals, and, thus, a repetition of their substance would be redundant. An experiment has been initiated recently, involving one aspect of the matter, namely, the examination of the relative rate and manner in which lead sesquioxide, dispersed in particles of comparatively large size (mean diameter of 0.5 micron) may be absorbed into the body, as compared to the same compound in much finer dispersion (mean diameter, 0.05 micron). In other experiments, the size of particles to which human subjects have been exposed have ranged from 0.75 to 1.2 microns (mean diameter).

Funds were made available, through the Lead Zinc Organization, for the conduct of this experiment, to begin promptly in 1970, but difficulties were encountered in securing a suitable subject for the experiment. Only in May was a subject, believed to be suitable for the purpose, found and employed (a young woman, Subject P.B.). The preliminary observations (for the purpose of establishing the pattern of the Subject's normal metabolism), initiated on May 10, 1970, have been under way since, and are to be continued as long as may be necessary to reveal this pattern (through two seasons, at least, so as to range through warm-hot and cool-cold environmental climatic conditions. No female has been employed previously as a subject for this type of experimentation, so that it is necessary to carry out the preliminary observations with unusual care, and to subject the early data to unusually critical examination, before initiating the exposure to the designated aerosol. (Not only was it difficult, at this time, to obtain the services of a

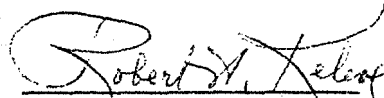
suitable male subject, but also, after confronting this situation, it became increasingly obvious that some portion, at least, of this general physiologic investigation should concern itself with a thorough-going examination of the metabolism of lead in the female human being. After the enforced fact, this opportunity is welcomed, especially at the present time, when the exposure to lead in the general environment has come to be a question of importance in the field of public health, as well as in the area of occupational health.)

As indicated previously, the duration of the exposure to lead is to be limited to eight (8) hours per day, on five (5) days per week, at the level of one hundred-fifty (150) micrograms of lead (Pb) per cubic meter of air, in simulation of the more or less standard industrial time schedule, but at the same level of concentration at which other observations have been made (which, in fact, was the accepted standard for reasonably safe occupational conditions at the time these experiments began). This part of the experiment will not be attempted before (or, at most, not much before) the end of 1970. It will extend into 1971, therefore, for a length of time which cannot now be determined precisely, but which will not be shorter than six (6) months and may well be longer.

The cost of carrying out the work now being done has been examined with some care and has been set down in one of the sheets (budget 1970) attached to this proposal. On another sheet is the estimated budget for 1971. No doubt some portion of the funds requested for 1970 will be available for use in 1971, and the actual sums of money provided for in the continuance of the project in 1971 can be regulated according to the desires of the sponsors. It is recommended, however, that provision be made for continued work throughout 1971, since a program can be submitted for another experiment in the series, which might well extend into 1972, conditional upon the advice and consent of the sponsors.

With respect to the suggestions made above, it is not presumed, at this time, that the work on the metabolism of lead will be continued indefinitely under

the present sponsorship, or that the present principal investigator will, necessarily, be the instigator of such continuation. This principal investigator, nevertheless, is of the firm belief that the facilities and capabilities within the Kettering Laboratory, as provided by considerable effort and investment, and seasoned by long experience, can be and should be further cultivated to the end that these investigations may be further advanced in the years to come. Lead is an extremely useful element in the technology, economy and comfort of mankind, and it should be as thoroughly understood, in its relation to human physiology, as the reasonable scope of scientific investigations can make it. The extent to which the present and future Staff of the Kettering Laboratory can penetrate further into the scientific and practical aspects of industrial and public health will depend largely upon the quality of the cultivation of the resources of the Laboratory. This proposal is conditional upon the desirability and practical importance of that end.

  
Robert A. Kehoe, M.D.

June 24, 1970

KE

04420

Values Reflecting Pb Intoxication  
in Humans

| <u>Criterion</u>                      | <u>Proposed Levels-URINE</u>    |                              | <u>Kettering<br/>Abstract<br/>Ref.</u> |
|---------------------------------------|---------------------------------|------------------------------|----------------------------------------|
|                                       | <u>Normal</u>                   | <u>Pathologic</u>            |                                        |
| <u>ALA</u><br>(exposed 10 to 15 days) |                                 | 5 to 10 times<br>normal      | I 41                                   |
|                                       | 2.5 mg/24 hr.                   | 19.07 mg/24 hr.              | I-66                                   |
| <1 yr. post exp.                      |                                 | 29 mg/24 hr.                 | I-75                                   |
| 1 to 3 yrs. "                         |                                 | 15 " "                       | "                                      |
| 3 to 9 yrs. "                         |                                 | 4.6 "                        | "                                      |
|                                       | 1.3 to 2.8 mg/24 hr.            |                              | "                                      |
| Based on creatinine<br>excretion      | 0.85 to 2.4 mg/g creat.         | >2.4 mg/g creat.             | I-259                                  |
| 24 hr. output                         | Up to<br>4 mg                   | Up to<br>110 mg.             | I-260                                  |
|                                       | 2.8 mg/24 hr.                   | 1.5 mg/100 ml                | II-116                                 |
|                                       | 4.53 mg/l                       | ~ 30 mg/l<br>> 3.0 mg/24 hr. | II-116<br>I-261                        |
| <u>PROTO</u>                          | 21.2 $\mu$ g/100 ml<br>TEL      | 512 $\mu$ g/100 ml<br>Tb     | I 53                                   |
| <u>COPRO</u>                          | 150 mg/l<br><100 $\mu$ g/24 hr. | up to 450 mg/l               | II-116<br>I-261                        |
| <u>PBG</u>                            | 1.5 mg/24 hr                    | 1.94 mg/24 hr.               | I-46                                   |

Proposed Levels-BLOOD

| <u>Criterion</u>  | <u>Normal</u>        | <u>Pathologic</u> | <u>Ref.</u> |
|-------------------|----------------------|-------------------|-------------|
| <u>ALA</u>        | 0.026 mg/100 ml(max) |                   | I-66        |
| <1 yr. Post exp.  |                      | 0.065 mg/100 ml   | "           |
| 1 to 3 yrs. "     |                      | 0.043 "           | "           |
| 3 to 9 yrs. "     |                      | 0.032 "           | "           |
|                   | 0.026 mg/100 ml      |                   | II-116      |
| <u>Plasma ALA</u> | 0.046 mg/100 ml      | 126.7 mg/100 ml   | I-66        |
| <u>Plasma PBG</u> | 0.030 mg/100 ml      | 0.029 mg/100 ml   | "           |

# Proposed Levels-BLOOD

Kettering  
Abstract  
Ref.

## Criterion

## Normal

## Pathologic

### RBC

Proto IX

ALA Dehydrase

PROTO IX

< 1 yr. Post exp.

1 to 3 yrs. "

3 to 9 yrs. "

volume

survival time

" "

0.035 to 0.055 mg/100 ml

1.03  $\mu$ M/hr/ml.

1.08  $\mu$ M/hr/ml

0.232 mg/100 ml.

0.225 "

0.159 "

reduced

reduced 37 to 69%

21 to 41 days

I-75

I-66

I-75

"

"

I-39

"

I 408

### BLOOD Pb

adults

children

0.08 mg/100 g

0.04 "

0.04 to 0.08

mentally deficient

I-290

"

adults

0.025 mg/100 g  
(0.005 to 0.040)

I-387

RBC vol.

Hgb

Hct.

MCV

MC Hgb conc.

Reticulocytes

Stippled cells-RBC

Icteric Index

$5 \times 10^6 / \text{mm}^3$

14.5 g %

45%

80 to 94  $\mu$

33 to 38 g/100 ml

0.5 to 1.5%

3 to 5

3.5 to  $5.4 \times 10^6 / \text{mm}^3$

8 to 12.8 g %

28.8 to 43% (35% ave.)

70 to 92 (79 ave.)

27 to 36 g/100 ml (31 ave.)

1.5 to 11.6% (4.4 ave.)

0.1 to 7.5% (1.8% ave.)

4 to 10 (6.5 ave.)

I-263

"

"

"

"

"

"

"

"

Stippled cells-REC

" " "

> 200/10<sup>6</sup> cells

> 0.5%

I-271

I 387

Sp. G. (blood)

1.057

(1.052 to 1.063)

< 1.054

I 387

# Proposed Levels-Miscellaneous

| <u>Criterion</u>                     | <u>Normal</u>                                    | <u>Pathologic</u>                                 | <u>Kettering<br/>Abstract<br/>Ref.</u> |
|--------------------------------------|--------------------------------------------------|---------------------------------------------------|----------------------------------------|
| Urinary<br>Aminoacetone              | 0.59 to 1.03 mg/g                                | within normal<br>limits                           | I 259                                  |
| Urinary Pb adults<br>non-precip.     | 0.002 mg/l                                       | 0.027 mg/l                                        | II-117                                 |
| precipitable "                       | 0.047 mg/l                                       | ↑absorption 0.100 mg/l<br>Pb intoxic. 0.204 "     | II-117<br>"                            |
| Total Pb-urine "                     | 0.049 mg/l                                       | ↑absorp. 0.127 mg/l<br>Pb intoxic. 0.300 "        | "<br>"                                 |
| Urinary Pb children                  |                                                  | 0.06 to 0.182 mg/l                                | I-88                                   |
| Tissue Pb adults<br>soft<br>skeleton | 0.04 to 0.28 mg/100 g<br>0.67 to 3.59 "          |                                                   | I-56                                   |
| Pb inhalation                        | 10 to 20 X more absorption.<br>than by ingestion |                                                   | I-256                                  |
| Spinal fluid                         | ~ 18 $\mu$ g/100 ml                              | ~ 25 to 50 $\mu$ g/100 ml<br>fatal cases: ~ 100 " | I-256                                  |