

used also with pencil addition, at L. de la J. J. J.
Apr 13, 1944

EXPERIMENTAL STUDIES ON LEAD ABSORPTION AND EXCRETION AND
THEIR RELATION TO THE PREVENTION, DIAGNOSIS, AND TREATMENT
OF LEAD POISONING

Introduction

General Procedure of Experiments

- | | | | |
|-----|--|---------|---------|
| | 1 year | 4 years | 2 years |
| (1) | Dosage of lead - normal diet - diet + 1 mg. $PbNO_3$ - diet + 2 mg. $PbNO_3$ | | |
| (2) | Collection of samples and analyses - 3 parallel methods | | |
| (3) | Medical observations | | |
| (4) | Microscopic observations on blood | | |

General Purpose of Experiments

- (1) To determine the safe limits of oral lead intake in food and beverages - General public health problem
- (2) To determine the physiological background of lead absorption, retention, and excretion, under conditions of maintained prolonged lead exposure, on a quantitative basis, and to answer certain immediate practical problems.
 - (a) The relationship between urinary lead excretion and the stream of continuing lead absorption.
 - (b) The relationship between urinary lead absorption and the quantity of lead in the body.
 - (c) The relationship between urinary lead excretion and alimentary lead excretion.
 - (d) The importance of lead absorption from the alimentary tract under the most favorable conditions of absorption.
 - (e) The fate of retained lead after discontinuance of lead exposure (and absorption).
 - (f) The effect of various factors on the rate of lead absorption and retention of lead, under conditions of prolonged lead exposure (and absorption).
 - (g) The effect of various factors on the rate of excretion of lead after discontinuance of lead exposure (and absorption).

Custom preliminary fact.

- Slide 1 - lead in food and feces*
2 - lead in blood
3 - lead in blood - normal
4 - " " urine - normal
5 - " " blood in cap. exp.
6 - lead in urine in cap. exp.

- Slide 1 - 1.*
7 - threshold
8 - urine
9 - threshold normal
10 - " " normal
11 - " " threshold
2 - lead poisoning

Summary of Results

Physiology of Lead Absorption and Excretion

On 2 mg. daily - urinary conc. increases in 23 months from 0.032 to 0.107 mg. per liter

- | | |
|---|---|
| <p>Causes</p> <p>(1) Daily absorption effective, no doubt, but constant, throughout, therefore, also</p> <p>(2) Excretion of retained lead is a factor</p> <p>(3) Further shown by the continued high excretion and blood con-</p> | <p>Urinary output increases from 0.037 to 0.136 mg. daily</p> <p>Blood concentration increases from 0.029 to 0.072 mg. per 100 g.</p> |
|---|---|

Approaching potentially dangerous levels
without illness
without lead line
without change in stippling

2. When 2 mg. daily discontinued; —

Urinary conc. drops off in 16 month
0.106 to 0.045 mg. per liter

Causes (1) Reduced daily absorption

(2) Slight progressive reduction of retained lead

(3) Relative redistribution of retained lead.

Rapid loss from soft tissue, slow from skeleton.

Possible but not probable because of time factor (16 months), with still elevated blood and urine levels

Urinary output drops off from
0.136 to 0.056 mg. daily

Blood concentration drops off from
0.072 to 0.036 mg. per 100 g.

Urine still to drop to normal levels

Blood still to drop to normal levels

3. Output and concentration vary with season

Slide 2 4. On 2 mg. daily Urinary output increases in 23 months from
1.00 mg. to 3.60 mg. per 28 day period

5. Varies with urinary volume (season)

Slide 3 6. On 2 mg. daily Fecal lead output jumps in few days
from 0.34 mg. to 1.94 mg. daily

7. When 2 mg. discontinued, - Fecal lead output drops in few
days to 0.32 mg. daily

There is no apparent lead excretion via
the alimentary tract at any time but only
passage of unabsorbed lead.

Slide 4 These facts shown graphically

Slide 5 8. Quantities of lead involved during administration
Quantity ingested - in water

in food
administered

Quantity eliminated - in feces
in urine

Quantity retained - about 8%

110 mg in 23 lunar months

- Slide 6
4 subjects
2 mg.
1 mg.
0.23 mg.
3 mg
9. Rate of accumulation constant on given regular dosage
Regularity of absorption, quantity of absorption, and
duration of absorption therefore, of primary importance.
10. Accumulation does not occur if dosage is sufficiently
small. See curve on Subject I.F. on intake of 0.23 Mg.
daily.
11. Calculated maximum dosage without accumulation between 0.5
and 0.6 mg.
- Slide 7
12. Quantities of lead involved after discontinuance of adminis-
tration when 2 mg. daily, discontinued, the quantity re-
tained decreased in 16 months from
110 to 70 mg. 40 mg lost in 16 lunar months, or 2.5 mg/mo (94% of dose)
with at least half the amount excreted by way
of the kidneys.
Any fecal excretion is questionable
as shown by facts on Subject M.R.
- Slide 8
- When 1 mg. daily, discontinued, the quantity retained de-
creased in 10 months from
118 to 111 mg. 10 mg lost in 10 lunar months or 1.0 mg/mo.
with somewhat more than this entire amount ex-
creted by the kidneys.
13. There can be no doubt that the most important
means of lead excretion is by way of the kidneys.
- Toxicity of Lead in Quantities Here Involved
- Slide 9
14. Threshold of toxicity in terms of urinary lead concentration
Industrial lead exposure
15. As shown by Cholak's data, concentration does not continue to
rise indefinitely but comes to a maximum characteristic of
the industry and its exposure.
Subject E.B. on 2 mg., on contrary, was still increasing at
0.11 mg. per liter when discontinued.
This level of lead absorption was greater, or else it was
more regular than that in a safe industrial occupation. In
any case it was safe for 2 years, but potentially unsafe if
carried on further, and was, therefore, discontinued. There
was, however, no clinical sign of lead absorption, or of
incipient intoxication, such as would justify transfer of a
workman from a dangerous job. The correctness of the con-
clusion of Sanders, with reference to the failure of stip-
pling to reveal significant lead absorption is clear.
- 16.
17. The actual absorption of lead daily, by indirect calculation,
approximated 1/10 of that ingested, i.e. about 0.13 daily
for Subject M.R. and about 0.24 daily for Subject E.B.
Both rates of absorption are probably dangerous if sufficient
time is allowed.

Alimentary Lead Absorption - How influenced?

no slide 18. By speed of alimentary emptying time.

Lead Retention - How influenced?

Slide 10 19. Following factors without influence at dosage of 1 mg. daily with absorption of about 0.13 mg. Pb per day.

- (1) Milk
- (2) Apple powder (pectin)
- (3) Vitamin C
- (4) Low Ca and P
- (5) Low Ca - high P
- (6) High Ca - Low P
- (7) High Ca - High P (Ca - Am - P in PM)

Slide 11 20. Same factors without influence on urinary output of lead except to extent of changes in urinary volume

Slide 12 21. Same factors without influence on fecal output of lead except to extent of changes in alimentary emptying time

Lead Loss from Body - How influenced?

22. By reduction in rate of daily absorption
By increasing or decreasing urinary lead excretion

Slide 13

- (1) By changing urinary volume
No other influence experimentally tested was of any avail.
- (2) Changes in acid-base equilibrium and gross increase in Ca and P output had no influence. NH_4Cl was effective only to the extent of its diuretic action and not by virtue of acid shift.

Repeat
Slide 1
Slide 2

The apparent increase in output, with changes in concentration occurred also at same time in subject E.B. as shown in Slides 1 and 2

Practical Applications

1. In relation to industrial lead exposure *and the prevention of lead poisoning*
 - (1) Threshold of Intoxication
Urinary Standard
 - (2) Dosage x time factor in exposure
Intermittent exposure and non-exposure
Intermittent accumulation and loss
 - (3) Importance of normal alimentation in relation to dosage of lead, by mouth or by inhalation
 - (4) Importance of adequate water intake and renal output
2. In relation to diagnosis of lead poisoning
 - (1) Lead exposure and absorption and clearly demonstrated by the levels of lead in the urine and blood, even for considerable periods after exposure has come to an end.

Either, Concentration or output in unit time will reveal the situation with reference to exposure KE 0008727

- (2) These reveal only the magnitude of exposure and absorption, but not illness
- (3) Fecal lead of no diagnostic significance except in relation to an existing source of exposure

3. In relation to treatment

- (1) Discontinue exposure
- (2) Keep bowels open
- (3) Give adequate fluids
- (4) Usefulness if "deleading" questionable
Apparently of little or no avail, at least within
limits of retention thus far studied by these methods.