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- | <u>General Procedure of Experiments</u> | | | |
|---|--|---------|---------|
| | 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 | | |

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- ### 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).

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1. On 2 mg. daily - urinary conc.increases in 23 months from 0.032 to 0.107 mg. per liter
- Causes (1) Daily absorption effective, no doubt, but Urinary output increases from constant, throughout, 0.037 to 0.136 mg. daily therefore, also
- (2) Excretion of retained lead is a factor Blood concentration increases from 0.029 to 0.072 mg. per 100 g.
- (3) Further shown by the continued high excretion and blood con-

continuance of
administration

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

2. When 2 mg. daily discontinued.

Urinary conc. drops off in 1 month
0.106 to 0.045 mg. per liter

Causes (1) Reduced daily absorption

Urinary output drops off from
0.136 to 0.056 mg. daily

(2) Slight progressive reduction
of retained lead

(3) Relative redistribution of retained lead. Blood concentration drops off from
0.072 to 0.036 mg. per 100 g.

Rapid loss from
soft tissue, slow
from skeleton.

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

8. Quantities of lead involved during administration

Quantity ingested - in water

in food

administered

Quantity eliminated - in feces

in urine

Quantity retained - about 8%

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Slide 6
3 subjects
2 mg.
1 mg.
0.23 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.
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.
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 kidney

Toxicity of Lead in Quantities Here Involved

14. Threshold of toxicity in terms of urinary lead concentratio

Slide 9

Industrial lead exposure

15. As shown by Cholak's data, concentration does not continue
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.E.
Both rates of absorption are probably dangerous if sufficient
time is allowed.

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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
- (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
NH₄Cl was effective only to the extent of its diuretic action and not by virtue of acid shift.
The apparent increase in output, with change in concentration occurred also at same time in subject E.B. as shown in Slides 1 and 2

Repeat
Slide 1
Slide 2

Practical Applications

1. In relation to industrial lead exposure
 - (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.

- (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.