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# THE EFFECT OF DIMERCAPROL ON LEAD POISONING IN MICE *

BY

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The published investigations of the effect of dimercaprol or 2 : 3-dimercaptopropanol (BAL) in lead poisoning in animals have been chiefly concerned with acute poisoning or with toxicity. Braun, Lusky, and Calvery (1946), Graham and Hood (1948), and also Germuth and Eagle (1948) reported that dimercaprol failed to protect animals poisoned with lead acetate, and that the dimercaprol-treated animals died sooner. In acute poisoning, Ginsberg and Weatherall (1948) found that dimercaprol increased the urinary excretion of lead, and altered the distribution in the organs. The present work was designed to estimate the effect of dimercaprol on the retention of lead in a more chronic form of plumbism.

## METHODS

The mouse was chosen as the experimental animal because the whole animal could be ashed and a determination of the total lead content made. Lead acetate was fed with a low calcium diet to male mice in such amounts that the maximum possible daily dose was 1 mg. Pb per mouse. The procedure followed was similar to that used by Tompsett (1939), who showed that retention of lead in mice was highest on a low calcium diet. The lead acetate in most experiments was marked with a tracer of $Pb^{210}$ (i.e., radium D). This naturally occurring isotope has the great advantage of being easily obtained from old radon tubes. The lead was fed for 8 to 14 days, and after varying intervals of time the animals were killed, the stomach and intestine removed and discarded, to remove any lead excreted into the gut, and the whole carcass ashed; the ash was brought into solution with the minimum of acid, and made up to 100 ml. with water. Lead was then estimated chemically in aliquots of the ash solution by the method described previously (Tompsett and Anderson, 1935). Where radioactive lead had been administered, the activity of the ash solution was estimated by means of a Geiger-Müller counter. In practice the $\beta$ radiation of radium D is too weak to count and the stronger $\beta$ radiation of radium E in equilibrium with radium D is counted. Ash samples had therefore to be kept until the mixture reached equilibrium, a matter of 30–40 days.

Dimercaprol dissolved in oil, or as a freshly prepared solution in saline, was injected subcutaneously in daily doses of 50 mg./kg. mouse, either during the entire period of administration of lead or in the subsequent period.

## RESULTS

The results obtained when dimercaprol was given simultaneously with the lead are shown in Table I. The first two experimental animals received dimercaprol in oil solution daily for eight days, the other three dimercaprol in saline for eleven days. The results of the chemical analysis show that the lead content of the mice receiving dimercaprol was significantly lower than that of the controls. There is not a very close agreement

TABLE I

ADMINISTRATION OF LEAD AND DIMERCAPROL (BAL) SIMULTANEOUSLY

Lead content of mice in mg./100 g. *a* by count. *b* by chemical analysis

| Controls | | Dimercaprol | | |
|---|---|---|---|---|
| *a* | *b* | *a* | *b* | |
| 1.0 | 1.08 | 0.39 | 0.31 | Lead 10 days |
| 0.96 | 1.20 | 0.63 | 0.56 | BAL in oil 8 days |
| 0.75 | 0.73 | 0.48 | 0.59 | Lead 14 days |
| 1.06 | 1.11 | 0.71 | 0.55 | BAL in saline 11 days |
| [1.92] | 0.89 | 0.40 | 0.42 | |
| Mean: 0.94 | 1.00 | 0.52 | 0.48 | |
| Range: | 0.73–1.11 | | 0.31–0.59 | |
| S.D.: | ±0.19 | | ±0.12 | |

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between the figures obtained by count and those by chemical analysis, but they are of the same order and serve as a useful check. For some unexplained reason one of the controls, in brackets, gave a very high count, and has been excluded from the calculation of the mean. The lead content is given here as mg./100 g., but as the dead weights were all of the same order the same conclusions are reached if one compares mg. of lead per mouse.

The lead given was approaching a lethal dose, as in some similar experiments one or more of the animals died during administration of the lead. When mice which had been fed lead previously were treated with dimercaprol the results shown in Table II were obtained. The first two experimental animals received dimercaprol in oil, and the next six dimercaprol in saline. This second series were fed non-radioactive lead. Three of the control animals and four of the treated died near the end of the experiment on the days shown. Two animals died before dimercaprol treatment was started and were not analysed. Treatment with dimercaprol had no significant effect on the final lead content. The figures for the second series show a wide variation owing to the variation in the dead weights in this series where older animals were used (the previous animals were all "20 g. mice"). If the actual amounts of lead found in the individual mice, as shown in Table III, are compared, it will be seen that the variation is less, and that dimercaprol had no significant effect.

TABLE II

ADMINISTRATION OF LEAD FIRST THEN DIMERCAPROL (BAL)

Lead content of mice in mg./100 g. *a* by count. *b* by chemical analysis

| Controls | | Dimercaprol | | |
|---|---|---|---|---|
| *a* | *b* | *a* | *b* | |
| 1.58 | 0.72 | 1.17 | 0.92 | Lead 8 days then 7 days |
| 0.98 | 1.08 | 0.89 | 1.04 | BAL in oil last 4 days |
| Mean: | 0.90 | | 0.98 | |
| | 0.53 | | 1.15 (17) | |
| | 0.95 (20) | | 0.95 (21) | Lead 10 days |
| | 0.41 | | 0.85 (20) | then BAL in |
| | 0.45 | | 0.50 (22) | saline 12 days |
| | — (12) | | 0.61 | |
| | — (12) | | 0.47 | |
| Mean: | 0.58 | | 0.75 | |

Numbers in parentheses indicate day of death.

TABLE III

LEAD FIRST THEN DIMERCAPROL

Actual lead content of mice in mg. from Table II. Chemical analysis

| Controls | Dimercaprol | |
|---|---|---|
| 0.18 | 0.23 | Lead 8 days then 7 days |
| 0.26 | 0.27 | BAL last 4 |
| 0.18 | 0.22 | |
| 0.19 | 0.24 | Lead 10 days |
| 0.16 | 0.21 | then BAL for |
| 0.18 | 0.15 | 12 days |
| — | 0.19 | |
| — | 0.16 | |
| Mean: 0.19 | 0.21 | |
| Range: 0.16–0.26 | 0.15–0.27 | |
| S.D.: ±0.035 | ±0.038 | |

## Discussion

Dimercaprol did not diminish the toxicity and more animals died in the experimental series than in the control. Germuth and Eagle (1948) have reported that the lead-dimercaprol complex is almost as toxic as lead itself.

Dimercaprol given during the exposure to lead caused less lead to be accumulated in the body, but how this was brought about, whether by an increase in excretion or by a decrease in absorption or by both cannot be determined from the evidence presented here. There is some published evidence that dimercaprol produces a temporary increase in urinary excretion of lead both in animals (Germuth and Eagle, 1948; Ginsberg and Weatherall, 1948) and in man (Ryder, Cholak, and Kehoe, 1947; Telfer, 1947).

The fact that dimercaprol had no effect on the loss of lead from the animals previously treated with lead for eight to ten days provides no support for its use in the treatment of chronic lead poisoning.

## Summary

1. Lead acetate marked with a tracer of $Pb^{210}$ (radium D) was fed with a low calcium diet to mice, and after varying periods the lead content of the whole animal was determined by chemical analysis and count of $\beta$ radiation.

2. The lead content of mice which had received 50 mg. dimercaprol per kg. daily, and lead simultaneously for 10 to 14 days, averaged 0.48 mg.

Pb/100 g. of mouse, and was significantly lower than that of controls receiving lead alone, which averaged 1.0 mg. Pb/100 g.

3. When lead alone was administered for eight to ten days, subsequent treatment with dimercaprol during a recovery period of one to two weeks had no significant effect on the final lead content.

4. These results provide no indications for the use of dimercaprol in treatment of chronic lead poisoning.

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