THE CONCENTRATION OF LEAD IN THE PLASMA OF HUMAN BLOOD IN RELATION TO EXPOSURE TO LEAD, LEAD INTOXICATION, AND THE ADMINISTRATION OF BAL

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It is commonly inferred that the concentration of lead in the plasma of the blood increases as it does in the whole blood, with an increase in the absorption of lead on the part of experimental animals or men. It has also been supposed that such an increase occurs in association with the onset and development of lead intoxication, ~~and~~ Smith and ~~their~~ his associates (1 ~~and Rathwell~~) believed they found evidence of such an increase. (Previous work in this field has been summarized by Bambach, Kehoe and Logan (1) in their study of the plasma-cell partition of lead in the blood of rabbits.) Analytical data gathered over a period of years seemed to justify doubt as to the validity of such inferences, and the matter has been investigated systematically by measuring the concentration of lead in the plasma of persons with different degrees of exposure to lead, with and without lead poisoning, and of men in whose blood the concentration of lead has been altered quickly by the administration of dithiopropanol (BAL).

The quantities of lead in samples of plasma obtained from the blood of four groups of men observed in the years 1943-1947 have been determined, and the results

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obtained on each occasion each man are plotted in figures 1a and 1b and 2a and 2b. In figures 1a and 2a, the samples are plotted arithmetically. It may be seen by inspection that the agreement between the two samples depends on the concentration of lead in the samples; the higher the concentration, the greater is the scatter about the line indicating 1 to 1 correspondence. Such data cannot be analyzed by statistical methods that depend for their validity on independence of the degree of scattering and the magnitude of the concentration. When the data are transformed to logarithms, the deviations from the regression are independent of the magnitude of the concentration (Fig. 1b and 2b). For such data these conventional statistical methods give efficient and unbiased estimates of the parameters that characterize the data. That the errors of the analytical methods are relative, rather than absolute, can be also visualized by expressing the amount found in sample A as the percentage of that found in sample B (Fig. 3).

The data from the second experiment are plotted logarithmically in figure 4. The distribution is of the same form as in figures 1b and 2b, with the scatter of the same order. The estimates of the parameters for the three groups of men, the three groups combined, and the total of all the spectrographic-dithizone differences are listed in table 3.

In this table columns 1 and 2 relate to the differences between consecutive samples as estimated by each method in the first experiment. In each case the mean lead concentration found in the first sample was less than that in the second; the means of the first samples were 98.2% and 99.3% of the second, on the average. Such differences are found frequently on the basis of chance, as shown by the "t" test. Each pair of samples A and B were analyzed the same day, although each sample was handled separately after it was collected; the absence of a significant mean difference by either method indicates that there is no contamination resulting from introduction of the needle into the vein; the blood samples are aliquots. The variances of the differences are of the same order; although the error of the dithizone method is less, the difference in the variances is not statistically significant ($F = 1.239$. $P > 20\%$). In this experiment the two analytical methods had the same relative order of accuracy.

Of importance is the fact there was a significant systematic difference between the two methods, (P = 0.[illegible]), the spectrographic method running 37% of the dithizone method, on the average. Examination of the original data (Table 1) shows this to be due in large part to the low spectrographic results on the five samples of "Pro", and the last three on "Hul", in both samples A and B. Samples analyzed spectroscopically on other men done the same dates were not uniformly low. The weight of the samples analyzed was average, and the concentrations of lead found were the same as those found in other men in the group. The samples taken for working were aliquots of those taken for the colorometric analysis: the discrepancy could not have been due to the drying, ashing and diluting of the samples. These two men had had a different type of exposure to lead than any of the other men; they had worked, without a mask, using air hammers and torches in dismantling a factory formerly used in the manufacture of white lead by the "Old Dutch" process. They were the only two men in this series with this kind of exposure.

No further samples than those listed in the table were obtained on Bro; Hul was studied for more than a year following his exposure, because of the persistence of symptomatology which the consulting psychiatrist stated was an emotional reaction precipitated by the episode of acute lead poisoning. These samples are listed in table 4. The samples were analyzed during a period of time that a number of samples from other men with varied degrees of exposure to different types of hazardous lead dust or fume were being analyzed in the laboratory each day, and in which no systematic difference between the methods was observed. In both of these men the systematic difference between the methods was of the same order, the spectrographic method averaging 70 and 76% of the dithizone method. The differences in all likelihood could not have been due to random sampling, since the probability of such an occurrence would have been less than 1 in a thousand in each case (Table 5).

We have no clinical explanation to offer for these remarkable findings. Their significance in the light of the problem at hand lies in the fact that they indicate that there occasionally are systematic differences between the two methods, and that such differences are far beyond the probable limits of random sampling deviations. Yet in absolute amount (+25%) they are small, when measured by the 5% fiducial limits* of a single sample by either method (±50%), by the range of variation of blood lead (0.01 to over 1.00 mg.%, over 10,000%), by the average difference between the blood lead of men without occupational exposure to lead and men with lead poisoning due to occupational exposure to lead dust and fume (0.045 and 0.25 mg.%, 1000%) and by the upper 2.5% fiducial limit of men without occupational exposure to lead and the lower 2.5% fiducial limit of men with lead poisoning due to occupational exposure to lead (0.05 and 1.0 mg.%, 100%).

Table 5 also indicates that in certain groups of men the spectrographic method gives systematically higher values than the dithizone method, and these differences are also statistically significant. In the group of poisoned men treated with BAL, in which this systematic difference was statistically significant, the differences favorable to the

* The 5% fiducial limits [illegible] single observation [illegible] [illegible] in the [illegible].

spectrographic method were rather uniformly distributed among the men, and independent of either BAL therapy, the amount of lead in the sample, the extent of the exposure to lead, or the presence or absence of lead poisoning. Such systematic deviations are most easily explained as due to an unusual, but not remarkable, random sampling effect (once in fifty times).

The comparison of the variances is of importance equal to the comparison of the means, for the variances are the measure of the errors of the methods. The smallest variances are those of the differences in the first experiment between the samples A and B when measured by either method. This is to be expected, for each pair of samples was analyzed the same day, and all the samples were analyzed within a period of two months. The variance of the dithizone method was smaller than that of the spectrographic method, but not significantly so (e^{2z}, or F, = 1.39, $P > 20\%$); therefore these variances may be combined to give a more reliable estimate of the variance of the differences. The combined variance of the erythrocyte samples is about twice this variance

Table 1

Employment Data on Insulating Crews in Various Localities
Including Those Selected for Study

Location	Date of Start of Operations	Number of Men in Present Crew Grouped as to Years of Exposure					Percentage Original Cr Now Employe
		Under 1	1-1.9	2-2.9	3-4	Total	
ast Orange, N.J.	May 1932			1*	4*	5*	100.0
ndianapolis, Ind.	June 1932				3	3	100.0
incinnati, Ohio	Nov. 1932	1		1	1	3	66.7
leveland, Ohio	Jan. 1933	1			2	3	66.7
ittsburgh, Pa.	March 1933	1		1	1	3	66.7
oston, Mass.	July 1933	1	1	2		4	25.0
hite Plains, C.	Nov. 1933	7*	3*	8*		18*	100.0
altimore, Md.	June 1934	1	4			5	80.0
lbany, N.Y.	Fall 1933	1*	2*	1*		4*	?
otal for All Localities Listed		13	10	14	11	48	
en Selected for Study (* Indicates Men Examined)		8	5	10	4	27	

Table 2

Dust Counts on Samples Obtained During Insulation of a Residence

Description of Sample	Volume of Sample in cu.ft.	Number of ~~Patients~~ Particles in Thousands per cu. ft. after subtracting bl	
		Average of three Counts	Average fo site
Sample #1, during hand packing near workmen at 5 ft. above floor.	5.5	310	220
Sample #2, during hand packing 2 ft. behind a workman at level of face	5.4	130	
Sample #1, during blowing 3 ft. behind a workman below level of face	4.93	6,000	7,100
Sample #2, during blowing 1.5 ft. to side of workman, at face level	5.0	8,200	
Sample #3, during blowing, at air pump during feeding, at face level.	10.0	760	

Table 3

Distribution of Men Engaged in Insulating Buildings with Eagle-Picher Rock Wool

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According to Age

Age in Years	Frequency
20 - 24	2
25 - 29	9
30 - 34	5
35 - 39	4
40 - 44	2
45 - 49	2
50 - 54	3
Total	27

Table 4

Distribution of Men Engaged in Insulating Buildings with Eagle-Picher Rock Wool

According to Systolic Blood Pressure

Mm. of Hg	Frequency
100 - 109	1
110 - 119	3
120 - 129	11
130 - 139	7
140 - 149	3
150 - 159	1
160 - 169	0
170 - 179	0
180 - 189	1
Total	27

Table 5

Distribution of Men Engaged in Insulating Buildings with Eagle-Picher Rock Wool

According to Diastolic Blood Pressure

Mm. of Hg	Frequency
60 - 64	1
65 - 69	2
70 - 74	3
75 - 79	3
80 - 84	7
85 - 89	4
90 - 94	6
95 - 99	0
100 - 104	0
105 - 109	1
Total	27

Table 6

Distribution of Men Engaged in Insulating Buildings with Eagle-Picher Rock Wool

According to Leucocytes in the Blood

Leucocytes per c. mm.	Frequency
6000 - 6900	2
7000 - 7900	5
8000 - 8900	11
9000 - 9900	3
10,000 - 10,900	2
11,000 - 11,900	1
12,000 - 12,900	1
13,000 - 13,900	1
16,000 - 16,900	1
Total	27

Table 7

Distribution of Men Engaged in Insulating Buildings with Eagle-Picher Rock Wool

According to Erythrocytes in the Blood

Erythrocytes per c. mm. in Thousands	Frequency
3100 - 3500	1
3600 - 4000	0
4100 - 4500	11
4600 - 5000	11
5100 - 5500	2
5600 - 6000	2
Total	27

Table 8

Distribution of Men Engaged in Insulating Buildings with Eagle-Picher Rock Wool

According to Hemoglobin Percentage of the Blood

Percentage of Hemoglobin	Frequency
80 - 84	3
85 - 89	0
90 - 94	4
95 - 99	5
100 - 104	13
105 - 109	0
110 - 114	2
Total	27

Table 9

Distribution of Men Engaged in Insulating Buildings with Eagle-Picher Rock Wool

According to the Occurrence of Stippled Erythrocytes in the Blood

Stippled Erythrocytes per Fifty Fields	Frequency
0 - 1	12
2 - 3	2
4 - 5	4
6 - 7	3
8 - 9	3
10 - 11	2
40	1
Total	27

Table 10

Distribution of Men Engaged in Insulating Buildings with Eagle-Picher Rock Wool

According to Lead in the Blood

Lead in Milligrams per 100 Grams Blood	Frequency
0.00 - 0.009	0
0.01 - 0.019	0
0.02 - 0.029	4
0.03 - 0.039	9
0.04 - 0.049	12
0.05 - 0.059	2
Total	27

Mean	0.044
Probable Error of Mean	±0.006
Standard Deviation	±0.008

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Table 11

Distribution of Men Engaged in Insulating Buildings with Eagle-Picher Rock Wool

According to Lead in the Urine

Lead in Milligrams per Liter of Urine	Frequency
0.00 - 0.009	0
0.01 - 0.019	8
0.02 - 0.029	4
0.03 - 0.039	4
0.04 - 0.049	1
0.05 - 0.059	1
0.06 - 0.069	2
0.07 - 0.079	1
0.08 - 0.089	1
0.09 - 0.099	1
No Information *	4
Total	27
Mean	0.037
Probable Error of Mean	±0.004
Standard Deviation	±0.025

*Four impossibly high results are not recorded since they were obviously contaminated in the process of collection.

Table 12

Distribution of Men Engaged in Insulating Buildings with Eagle-Picher Rock Wool

According to Arsenic in the Urine

Arsenic as As_2O_3 in Milligrams per Liter of Urine	Frequency
0.00 - 0.009	8
0.01 - 0.019	3
0.02 - 0.029	2
0.03 - 0.039	1
0.04 - 0.049	2
0.05 - 0.059	3
0.06 - 0.069	1
0.07 - 0.079	1
0.10 - 0.109	1
0.12 - 0.129	2
0.16 - 0.169	1
No Information *	2
Total	27
Mean	0.043
Probable Error of Mean	±0.006
Standard Deviation	±0.044

* Two samples were of insufficient volume for the analysis.

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