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MEASUREMENT OF INDUSTRIAL LEAD EXPOSURE BY ANALYSES OF BLOOD AND EXCRETA OF WORKMEN*

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EARLIER papers from this laboratory have given the occurrence of "normal" lead (1, 2, 3) and have shown the relationship of the concentration of lead in the blood and excreta of workmen to their lead exposure in a number of industries (4, 5, 6). Since the publication of these papers, similar observations have been made in other industries and additional data have been collected on some previously studied. During this period also the precision of the analytical methods has been increased, the general methods of study have been improved, and the physiological background of human lead absorption and excretion has been explored in some detail. Therefore the data now available may be expected to give a clear presentation of relationships which hitherto could be seen only in outline.

ANALYTICAL METHODS

As the reliability of the data depends partly upon the analytical methods employed and partly upon the manner of collecting samples, a brief discussion of these aspects of the work will be presented, special attention being given to factors which are frequently overlooked. In order to reduce opportunities for contamination with lead to a minimum, it is essential to scrutinize carefully every detail of the collection and preparation of samples. In addition to the purely chemical factors, the type of containers used and their chemical cleansing must be considered and also the care taken in the actual collection of the specimens. The latter should never be collected in the working areas or while the subject is in his working clothes. Contamination from factory dusts is frequently very serious; in one instance which has come to our attention, a laboratory had to discontinue urinary lead determinations because of this factor. Indeed difficulties associated with dusts from almost any source are considerable and are of such importance generally as to make it impossible to carry out analytical work of high precision unless atmospheric dusts are eliminated by means of an efficient dust-removal system in the laboratory.

In the case of blood specimens, it has been found necessary to employ all-stainless steel needles and Pyrex glass syringes, sterilized in all-glass vessels, in order to avoid frequent and serious contamination. The chief source of this contamination was traced to the use of the generally available needles made by pressing a steel tube into a hub of screw-cutting brass. The friction of the stylet against the opening in the hub frequently loosened minute particles of brass which were carried by the blood into the container. Other opportunities for significant contamination occur as the result of slight faults in the technique of drawing and handling blood samples, and it has been found to be a good practice to take two samples for analysis. In case of marked disagreement between the two results, the lower value is generally considered the true one since losses of lead are of much rarer occurrence than contaminations. If need be, additional samples are obtained.

Several excellent analytical methods are available, but for best results that chosen should have general rather than specific applicability. The dithizone (7, 8), spectrographic (9, 10), and polarographic (11, 12) methods that we have developed and described have approximately equal sensitivity and precision. Two of them, the spectrographic and dithizone methods, have been used interchangeably for a number of years, while the recent use of the polarographic method has added a further source of parallel results. The choice of any of the above methods for a particular problem is largely a matter of convenience, based upon the availability of equipment and the experience and preference of the analyst. (The recent statement of Fairhall and Keenan (13) that "the usual diphenylthiocarbazone procedure as carried out with small samples of urine gives high results," is at variance with the experience of competent analysts employing methods described by Wilkins, Willoughby and co-workers (14, 15), Clifford and Wichman (16), Hubbard (7), and

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Bambach (8). Since the details of the dithizone method that yielded high results in the hands of Fairhall and Keenan were not given, it is not possible to determine the reason for these high results.)

Justification for the use of these methods interchangeably is given in Tables 1 and 2. In Table 1 are listed the findings obtained by the spectrographic and dithizone methods on duplicate weekly blood samples from two subjects under experimental study. The general agreement between the two sets of results is apparent and offers convincing proof of the adequacy, not only of the analytical methods but also of the precautions taken in collecting and preparing the samples. The suitability of the polarographic method for this work may be gauged from Table 2 where results obtained by this technique, following isolation of the lead by two different methods, are compared with the spectrographic and dithizone findings from the same samples of human tissues. When three methods, based on entirely different principles, yield such closely concordant results, one can only conclude that the methods are specific and precise as applied.

TABLE 1

LEAD DETERMINATIONS ON CONSECUTIVE WEEKLY BLOOD SAMPLES OF TWO SUBJECTS MADE BY SPECTROGRAPHIC (10) AND DITHIZONE (8) METHODS

MG. Pb/100 GM.	SUBJECT M. R. FREQUENCIES		SUBJECT E. B. FREQUENCIES	
	Spectrographic	Dithizone	Spectrographic	Dithizone
0.0250–0.0299			5	3
0.0300–0.0349	3	1	0	2
0.0350–0.0399	12	3	7	5
0.0400–0.0449	26	6	8	3
0.0450–0.0499	25	16	4	9
0.0500–0.0549	24	38	17	10
0.0550–0.0599	19	31	16	15
0.0600–0.0649	20	24	22	24
0.0650–0.0699	13	14	4	12
0.0700–0.0749	8	16	5	12
0.0750–0.0799	3	4	5	3
0.0800–0.0849	1	0	8	5
0.0850–0.0899	0	2	1	
0.0900–0.0949	0	0	1	
0.0950–0.0999	0	1		
0.1000–0.1049	2	0		
Total.....	156	156	103	103
Mean.....	0.054	0.058	0.058	0.059
Probable error.	±0.001	±0.001	±0.001	±0.001
Standard deviation.....	±0.012	±0.010	±0.014	±0.013
Coefficient of variability...	±23%	±17%	±25%	±21%
Median.....	0.053	0.057	0.058	0.061
Mode.....	0.051	0.055	0.058	0.065

TABLE 2

LEAD DETERMINATIONS ON HUMAN TISSUES MADE BY THE SPECTROGRAPHIC, DITHIZONE, AND POLAROGRAPHIC METHODS

TISSUE	WEIGHT IN GM.	LEAD IN MILLIGRAMS PER 100 GRAMS			
		By Spectrographic Method (10)	By Dithizone Method (8)	By Polarographic Method (12)	
				Electrolytic Isolation and Concentration	Combined Extraction and Electrolysis
Spleen.....	28.4	1.05	1.18	1.12	1.10
Heart.....	30.1	0.050	0.032	0.035	0.045
Suprarenal.....	6.0	0.24	—	—	0.20
Stomach.....	26.5	0.085	0.095	0.080	0.070
Lung.....	49.0	0.39	0.40	0.36	0.35
Muscle.....	29.0	0.045	0.03	0.025	0.035
Thyroid.....	4.5	0.62	—	0.57	—
Small intestine...	18.5	0.070	0.060	0.06	0.065
Rib bone.....	6.5	16.85	17.7	17.1	18.2

Note that in most cases the aliquants employed represent very small quantities of material, so that the differences between the results often amounted to no more than 1 microgram.

RESULTS AND DISCUSSION

The interpretation of analytical results must be based upon reliable information on the concentrations of lead in the blood and excreta of persons without any industrial lead exposure. Illustrative data of this type are detailed in Table 3. Several groups of people of different nationalities have been studied by random sampling, and a number of individuals have been followed for long or short periods. For the sake of simplicity the probable errors and standard deviations are given only for the combined group. The mean value for the entire group has been influenced unduly by inclusion of a large number of samples from a few individuals. However, this figure is not far from that obtained in the case of random samples from a large number of individuals. The mean values

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TABLE 2

NS ON HUMAN TISSUES MADE BY GRAPHIC, DITHIZONE, AND OGRAPHIC METHODS

IGHT GM.	LEAD IN MILLIGRAMS PER 100 GRAMS			
	By Spectrographic Method (10)	By Dithizone Method (8)	By Polarographic Method (12)	
			Electrolytic Isolation and Concentration	Combined Extraction and Electrolysis
1.4	1.05	1.18	1.12	1.10
1.1	0.050	0.032	0.035	0.045
1.0	0.24	—	—	0.20
1.5	0.085	0.095	0.080	0.070
1.0	0.39	0.40	0.36	0.35
1.0	0.045	0.03	0.025	0.035
.5	0.62	—	0.57	—
.5	0.070	0.060	0.05	0.065
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TABLE 3

MEAN LEAD CONCENTRATION IN THE BLOOD, URINE, AND FECES, IN THE CASE OF NORMAL INDIVIDUALS AND GROUPS

DESCRIPTION	URINE		BLOOD		FECES	
	Number of Persons or Samples	Mg. Pb/L	Number of Persons or Samples	Mg./100 ml.	Number of Persons or Samples	Mg. Pb/24 hr.
Group A						
Frenchmen	33	0.030				
Mexicans	29	0.022	30	0.023		
Americans	30	0.029	30	0.027		
Germans	13	0.027				
Group B						
Normal Subject E. B.	56	0.031	9	0.029	54	0.346
Normal Subject M. R.	30	0.021	6	0.038	21	0.436
Normal Subject H. D.	551	0.021	76	0.034	537	0.265
Normal Subject I. F.	310	0.038	37	0.031	213	0.244
Combined Groups and Individuals						
Number	1,052		188		825	
Mean		0.027		0.030		0.270
Probable error		±0.0003		±0.0005		±0.003
Std. deviation		±0.014		±0.009		±0.145

on individuals merely illustrate the variability encountered thus far among normal persons.

The origin of most of this lead in "normal" persons has been discussed in detail in previous papers (1, 2, 3). Other sources are indicated in Table 4, in which are given some of the data of an incomplete study of the composition of air and fallen soot from a number of locations in Cincinnati. These results are merely illustrative and are not necessarily representative of atmospheric environment of cities in general or even of this community, since the range of values may shift considerably when more extensive data are available.

Comparison of the results obtained on normal persons with those arrived at in industrial studies (Table 5) is particularly illuminating, since there is a definite trend toward higher concentrations of lead in the urine, feces, and blood as the severity of known exposure increases. The increase in the urinary lead is obviously much more regular than that observed in the case of feces, and it is apparent that urinary and blood findings provide better criteria of lead exposure than fecal, especially under conditions of exposure to volatile and finely divided lead compounds (fume). On the other hand, when the predominant lead exposure occurs through the inhalation of dusts, the greater portion of the lead finds its way into the feces and gives evidence of the severity of the exposure. As is illustrated by the results (Table 5), the fecal values are likely to be spotty, only those in industries definitely associated with lead dusts showing

TABLE 4

PARTICULATE LEAD IN CINCINNATI AIR AND TOTAL LEAD IN CINCINNATI SOOTFALL

ELECTROSTATIC AIR SAMPLES (1941–)		SOOTFALL (1941–)	
Mg./10 Cu.M.	Number	% Pb per Ton of Soot	Number
0.000–0.019	16	0.000–0.039	10
0.020–0.039	37	0.040–0.079	14
0.040–0.059	11	0.080–0.119	5
0.060–0.079	5	0.120–0.159	7
0.080–0.099	6	0.160–0.199	8
0.100–0.119	2	0.200–0.239	6
0.120–0.139	1	0.240–0.279	2
0.140–0.159	1	0.280–0.319	5
0.160–0.179	1	0.320–0.359	0
0.180–0.199	1	0.360–0.399	1
0.200–0.219	1	0.400–0.439	1
0.220–0.239	1	0.520–0.559	1
0.240–0.259	0	0.600–0.639	1
0.260–0.279	1	0.720–0.759	1
Total	84	Total	62
Mean	0.051 ± 0.004	Mean	0.161 ± 0.012
Standard deviation	±0.051	Standard deviation	±0.145
Coefficient of variability	99.52%	Coefficient of variability	90.06%
		Mean sootfall per square mile for 1932–1939 equalled 15.3 tons	

marked elevation of the fecal lead. In a few instances (Table 5), insufficient material was available to establish stable mean values so that the results are tentative. The blood value listed for the white-lead group may be considered to be somewhat low since the mean was calculated from findings on blood samples taken at variable intervals after the exposure had ceased.

In spite of the significant differences between the means for unexposed and exposed persons, there is an overlapping of the results. The interpretation of individual findings within the overlapping range is always a matter of doubt, but the occurrence of overlapping is not remarkable, if viewed in the light of Figure 1. Here the data on large representative groups of unexposed persons and on employees in three industries are plotted so as to show the distribution percentage of each group within certain levels of concentration. The curves vary in height and shape. From the mean values and standard deviations obtained for the normal group, concentration ranges are obtained which can be used as bases of comparison with other groups. Thus in the case of urine it is seen that 90%, 50%, 14%, and 5% of the results in the case of unexposed persons, garage mechanics, men employed in the manufacture of tetra-ethyl lead, and men engaged in the manufacture of lead shot, respectively, are below 0.04 mg. lead per liter of urine. In the case of the results on the blood of the same groups, 90%, 80%, 50%, and 18%, respectively, are found at or below 0.04 mg. per 100 g. blood, while in the case of feces, the respective percentages for the same groups are 92%, 65%, 70%, and 17% at or below 0.45 mg. lead per sample of feces. A somewhat corresponding range of variability can be expected to occur as the result of repeated observations on the same individual, and therefore, by means of a sufficient number of observations, any person or group can be fitted into the proper place with respect to the level of the current lead exposure. Only a small number of observations are required if the individual in question belongs in either the unexposed or the heavily exposed groups.

The atypical character of exposure to tetraethyl lead, as contrasted with that associated with inorganic lead dusts, is shown best by the fecal findings, the percentage of values below 0.45 mg. being almost as great as in the case of persons without any industrial lead exposure.

A stable mean value for the urinary lead usually serves as a satisfactory measure of the overall exposure in an established industry, but much

TABLE 5

MEAN VALUES FOR LEAD IN URINE, BLOOD, AND FECES OF GROUPS OF PERSONS UNDER VARYING CONDITIONS OF LEAD EXPOSURE

OCCUPATION	MEAN VALUES					
	Urine		Feces		Blood	
	Number of Persons or Samples	Mg. Pb/L	Number of Persons or Samples	Mg. Pb/24 hr.	Number of Persons or Samples	Mg. Pb/100 g.
No occupational lead exposure	1,052	0.027	859	0.280	188	0.030
Applying insulation	23	0.037			27	0.037
Garage mechanics	654	0.050	463	0.486	145	0.039
Paint manufacture	20	0.067	20	0.505	20	0.048
Soldering	74	0.074			15	0.050
Gasoline pump repair	17	0.074			17	0.041
Manufacture of insecticides	27	0.079	26	0.546		
Manufacture of tetraethyl lead	762	0.093	750	0.458	136	0.045
Manufacture of lead shot	38	0.124	38	1.421	13	0.062
Manufacture of pigments	12	0.124	6	0.500	7	0.086
Brass foundrymen	60	0.161	55	0.592		
Manufacture of storage batteries	69	0.182	71	2.530		
Manufacture of white lead—moderate exposure	86	0.241	85	3.760	21	0.086
Manufacture of white lead—severe exposure	10	0.336	10	7.600		

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	15	0.050
	17	0.041
0.546		
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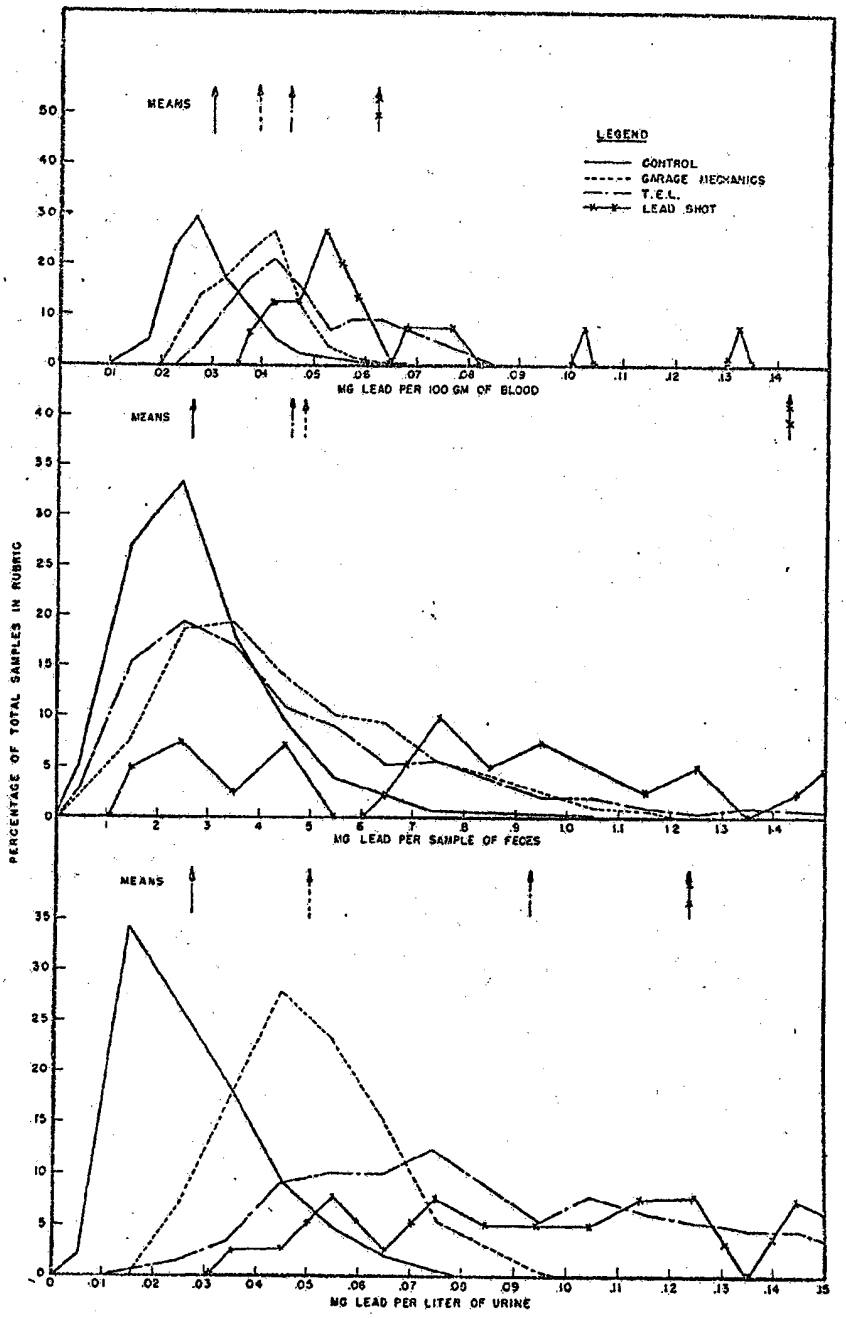

FIG. 1. Distribution percentages of lead concentration in urine, blood and feces for representative groups of normals and employees of three industries with lead exposure.

additional information may be gained by setting up the data in the form of histograms as indicated in Figure 2. The histograms recorded here characterize the total exposure of a certain plant (Curve V), and that associated with each of a series of individual occupations within the plant (Curves IV, III, II, and I). The histogram for the entire industry is fairly regular, but there is some skewness, which shows that several degrees of exposure are present. The composite character of this

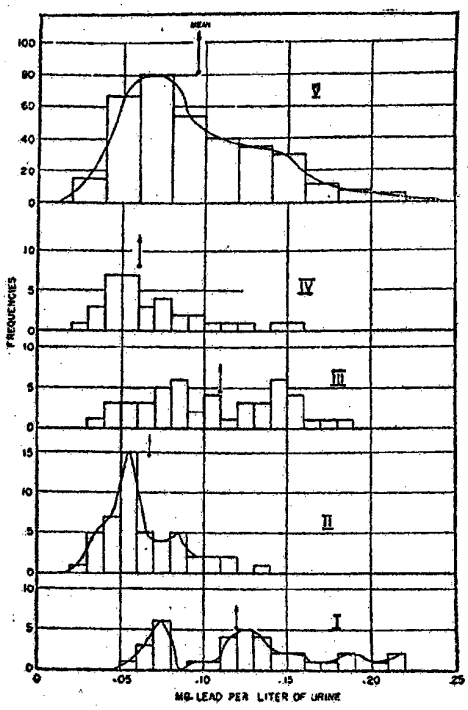

FIG. 2. Lead exposure in an entire plant and in industrial occupations within the plant as demonstrated by urinary lead excretions of representative workmen.

histogram is analyzed by means of the lower curves. The majority of the workmen have a relatively slight exposure, as is indicated by the close-to-normal distribution obtained for workers represented in Curves II and IV. However, other occupations in the plant are accompanied by greater exposure. (The severity of the exposure may also be affected by the personal habits of the men.) In the case of the men represented in Curve III, the high variability is an expression of irregularly occurring exposures of a relatively severe type. In Curve I, two modal groups are seen, as a clear indication that there are two universes of exposure. This may be due to two types of occupation within the group, or to the fact that some individuals were more careful in following precautions, thereby reducing the severity of their exposure.

Finally, such data, particularly the mean concentrations calculated from analytical results of periodic examinations of suitable numbers of representative workmen, can be used to detect changes in the exposure in a plant and also to compare different plants in the same industry.

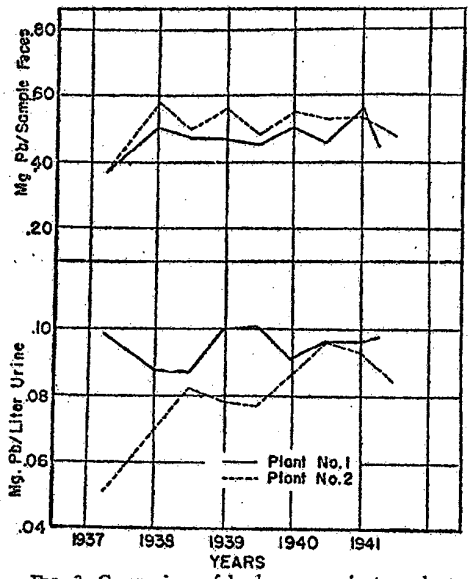

FIG. 3. Comparison of lead exposure in two plants of Industry A.

An example is given in Figure 3 where the mean values for lead in the urine and feces of workmen from two plants of the same type are plotted on a semi-annual basis for a number of years. The means for urinary lead in employees of plant No. 1 which has been in operation for a long time, are practically stable, at a level of 0.095 mg. per liter. On the other hand, the corresponding means for the workmen from the more recently opened plant No. 2, progressively increased for almost three years until finally the level approached that of plant No. 1, where it also may be expected to become stable. The initial mean urinary lead

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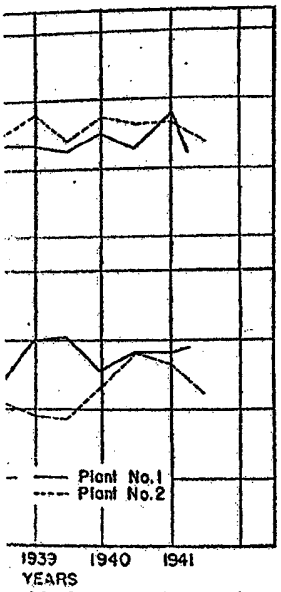

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concentration of the workmen in plant No. 2 at the start of operation is somewhat higher than that obtained for unexposed persons, in keeping with our observation that industrial employees in general yield somewhat higher values than office workers. From the study of the conditions of exposure as well as the precautions observed in these plants, it can be assumed that the degree of lead exposure was about the same in both of them. Therefore, the rise in the mean concentration of lead in the urine (plant No. 2), is the result of the cumulative absorption of lead during a period of essentially constant lead exposure, while the stable maximum level is characteristic of this industry with the safeguards that have been instituted.

An additional practical point of some importance is illustrated by the curve for plant No. 2, in that it may be seen that the maximum effects of occupational lead exposure are not reached for some time. The length of time required depends upon the type and severity of the exposure, and therefore lead determinations must be made periodically until stable mean values have been attained, if they are to reveal the maximum level.

The fact that the means for fecal lead in the two plants are practically in agreement and are at a constant level only slightly above the value of 0.45 mg., the upper limit for persons without industrial lead exposure, indicates that the exposure to lead dust is not great.

Conclusions

In the case of normal persons with no occupational lead exposure the mean lead concentrations are found to be 0.030 mg. per 100 g. blood, 0.027 mg. per liter of urine, and 0.27 mg. per 24-hour fecal sample. Exposure to lead in industry causes a definite increase in the mean lead concentration in these materials, in proportion to the severity of the exposure. The lead content of either the urine or the blood serves as a better criterion of lead exposure than does that of the feces. Analytical data from large representative groups of workmen may be set up in the form of histograms in order to determine the character of the exposure in a plant and particularly to show, from the modal groups, whether the exposure is uniform in type and severity. The distribution of results and the mean values obtained over extended periods of time can be used as a measure of the uniformity and efficacy of the means employed to control the lead exposure.

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