Reprinted from Occupational Medicine
February 1947, Vol. 3, pp. 156-171

EXPOSURE TO LEAD

ROBERT A. KEHOE, M.D.
CINCINNATI

IN SPITE of the amount of time spent in this conference on the discussion of this problem, the subject has not been covered in such a manner as to provide for the practical application of the best and fullest information now available. This effort has illustrated the difficulties of covering such a many-sided subject in a session of this type.

It is my function at this point to try to summarize the information, to try to make certain factual interpretations of the information so far presented and to bring this discussion into a well rounded state so as to bear with greatest practical efficacy on the problems which we, as industrial physicians and practicing physicians and industrial hygienists, have to meet. That is an extremely difficult assignment, and I have not the slightest hope that I shall be able to do it. I shall have to exercise my own judgment in the addition of certain facts to the discussion, and shall try to emphasize what in my own mind are the high spots in the practical application of the huge mass of information, inadequate as it is, that is available on this subject.

In doing this I shall try to stick to three principal headings: (1) the significance of the exposure of the public to lead, (2) certain aspects of industrial exposure to lead and (3) the problem of diagnosis.

THE SIGNIFICANCE OF EXPOSURE OF THE PUBLIC TO LEAD

I call your attention to a group of data in table 1, obtained in an incomplete attempt to picture for one area, and for only a few spots in that area, the lead content of the air. I shall not draw any conclusions as to the applicability of these results to the quantities of lead inhaled generally by persons in the population, but these samples were taken within the breathing zone of persons within this area. A more comprehensive study of this problem will be carried out in the future, but these are a few of the data which bear on it. A person in Cincinnati may be exposed to quantities of lead in the air respired during twenty-four hours, to an extent which is of about twice the order of magnitude

---

From the Kettering Laboratory of Applied Physiology, University of Cincinnati College of Medicine.

Presented in the Conference on Lead Poisoning at the Seventh Annual Congress on Industrial Health, Boston, Sept. 30, 1946.

of the figures given. Presumably, therefore, in the course of one day one is breathing in about 0.1 mg. of lead. Much of this is extremely finely divided. The amount actually absorbed is entirely a matter of conjecture. In following certain persons in otherwise approximately balanced experiments on the intake and output of lead, my colleagues and I have been able to find evidence of an imbalance which is the result of this inhalation of lead in the course of the day. The quantities represented from day to day, however, cannot be determined by the methods so far employed. In order to be more explicit, let me state the case in other words. In carefully controlled experiments on human metabolism we have found that over a period of six or eight months or a year, the normal healthy adult puts out a little more lead than he ingests in his food and drink, and although the quantity is small, the

TABLE 1.—*Particulate Lead in the Atmosphere*
Cincinnati, 1941

Lead, Mg. per 10 Cu. M.	Frequencies of Occurrence of Quantities of Lead Indicated
0 - 0.019	16
0.020 - 0.039	37
0.040 - 0.059	11
0.060 - 0.079	5
0.080 - 0.099	6
0.100 - 0.119	2
0.12 and over	7
Total	84
Mean	0.051
Probable error	±0.004
Standard deviation	±0.051

consistency with which it occurs is such as to demonstrate that there is an additional source of lead intake and absorption. This source, obviously, is to be found in the inhalation of the lead that has been shown to be present in the atmosphere. The origin of such lead is manifold. Time will not permit discussion of this point.

The next set of data, in table 2, brings me to the subject of food and to a brief and cursory reference to the problem of public health related thereto. As we have shown previously in experiments involving lead intake by mouth and lead output in feces and urine, the quantities which appear in the feces from day to day bear a close relationship to those occurring in the food from day to day. It is obvious that only a small proportion of ingested lead is absorbed. The result depends, in some degree, on the solubility of lead in the alimentary tract. In experiments of this type in which solutions of lead salts have been administered in known quantities to human subjects, we have found that something like 10 per cent of the lead is absorbed. This represents a greater proportional absorption than would be anticipated under ordinary circumstances. By and large, the degree of variability in the daily intake of lead in the food and drink and in the daily output in the feces, as shown in table 2, is fairly representative, and the mean values are characteristic of those found in the case of large groups of normal persons in the general population.

Now the point of these facts, for the purposes of present discussion, is that the situation illustrated by these data has existed for well over ten years with practically no change that could be demonstrated. It is about time to repeat our observations and to see whether anything has happened during and since the war to change this picture qualitatively or quantitatively, but it has been so stable for such a period of time that nothing remarkable is to be anticipated.

TABLE 2.—*Daily Occurrence of Lead in the Food and the Corresponding Feces of Three Normal American Adults with No Occupational Lead Exposure*

Lead, Mg. per 24 Hours	Frequencies of Occurrence of Quantities of Lead Indicated					
	In Food			In Feces		
	M. R.	E. B.	H. D.	M. R.	E. B.	H. D.
0 - 0.099	..	..	4	7	3	8
0.10 - 0.199	12	11	59	1	11	37
0.20 - 0.299	7	13	42	6	12	42
0.30 - 0.399	8	13	10	5	13	25
0.40 - 0.499	1	12	3	2	6	4
0.50 - 0.599	1	4	1	4	6	1
0.60 and over	2	3	2	6	5	4
Totals......	31	56	121	31	56	121
Mean..............	0.270	0.352	0.220	0.377	0.338	0.247
Probable error.....	±0.017	±0.016	±0.007	±0.037	±0.016	±0.007
Standard deviation	±0.137	±0.181	±0.110	±0.301	±0.172	±0.121

It is important to recognize that these physiologic observations have provided a means of studying the population on a broad basis. It will not be difficult to establish the essential facts with reference to the alimentary lead exposure of representative groups in the population of any community through the proper application of these methods.

Table 3 shows a simple application of this method in that samples of feces, representing roughly twenty-four hour evacuations, have been obtained from a series of persons and the results tabulated according to the frequencies of their occurrence. The mean value for this large number of samples is a familiar figure, being about one third of 1 mg. The fact was mentioned this morning that the present limit for lead in certain specific items of food amounts to about 7 parts per million by weight. If all foods were contaminated with lead to this extent, adults would be taking in average amounts of 14 or 15 mg. per day.

This brings me to the question of permissible limits for the contamination of food materials with lead and how the safety of the community can be guarded by the acceptance and enforcement of such tolerances.

It is clear that if every producer of food materials were to exercise the right of having his product contaminated to the extent permitted in some instances, the community would be seriously endangered. The tolerance applies to apples, on the theory that lead-containing insecticides must be employed to secure a crop. The concentration of lead in

TABLE 3.—*Lead Content of Random Samples of Feces of Normal Persons from Ten Widely Scattered North American Cities*

Lead, Mg. per Sample of Feces	Frequencies of Occurrence of Quantities of Lead Indicated
0 - 0.199	26
0.20 - 0.399	43
0.40 - 0.599	17
0.60 - 0.799	7
0.80 - 0.999	2
1.00 - 1.199	4
1.20 - 1.399	2
2.00 and over	1
Total	102
Mean	0.398
Probable error	±0.021
Standard deviation	±0.310

most of the other foods and beverages is low. It is important to remember these facts in relation to this general problem.

The data of table 4 show the facts in relation to water and certain other beverages. The drinking water in most North American cities contains lead to the extent of about 0.02 to 0.03 mg. per liter. Excep-

TABLE 4.—*The Lead Content of Various Beverages in the United States*

Substance	Source	Range of Analytic Results, Mg. per Liter	Number of Samples
Water	36 scattered cities	0.003- 0.04 (mean 0.01)	37
Water	Cincinnati	0.01 - 0.05	10
Water	New building	0.37 - 0.92	3
Coffee	Prepared for use	0.01 - 0.03	2
Milk	Cincinnati market	0.02 - 0.04	3
Beer	Cincinnati market	0.01 - 0.09 (mean 0.04)	21
Beer	Cincinnati market	0.13 - 0.29	3
Grape juice	Cincinnati market	0.04 - 0.4	7
Wine	Domestic and imported	0.05 - 1.51	10

tions to this condition may be found by taking samples of water from the mains of new buildings, as is illustrated in the data. The hot and cold water lines in the building were of the usual type, with no lead pipe at any point. However, unwittingly, the joints of the pipe were luted with a lead-bearing compound. When water was allowed to stand overnight in these pipes, it was contaminated to the extent of 0.39 to 0.92 mg. per liter. If the water flowed freely from the taps for ten or fifteen minutes the lead content dropped to 0.03 mg. per liter. This situation has probably occurred in connection with extensive building projects involving large numbers of houses, and under these conditions it may have more than minor or temporary importance. In general, however, the condition is fleeting and intermittent, and is not of great practical importance.

As to other beverages, only a few samples of many available have been given. The question of the generally accepted tolerance of 0.1 mg. of lead per liter arises. In my opinion, while this tolerance does not permit undue hazard under ordinary circumstances, it is too high for that segment of the population, wherever it may be, that is required to take in much larger than ordinary quantities of water per day in order to maintain water balance. Persons who must live and work

TABLE 5.—*Concentration of Lead in the Bones of Persons Believed to Have Had No Occupational or Unusual Lead Exposure*

Identification	Age, Years	Concentration of Lead in Mg. per 100 Gm. of Fresh Bone	
		Rib	Femur
E. S.	3	....	2.22
Girl	6	1.02	1.14
E. J.	20 ?	1.11	....
E. H.	51	0.47	....
N. R.	64	....	0.80
A. P.	70	0.39	3.59
J. W.	75	0.60	2.89
A. C.	95	0.56	1.36

at high temperatures may increase their water intake many-fold. Under these circumstances, if the situation were continued there might well be a potentially dangerous intake of lead. It is much better that drinking water should be as carefully controlled as it is at the present time and maintained within the limits which prevail commonly.

There is one other point of some consequence in relation to this general problem. The idea has existed over a considerable period of time that lead accumulates in the body irrespective of the rate of daily absorption, as long as some exposure and absorption occur. The evidence of our experimental work over the last several years has been such as to indicate that under the conditions of the normal or incidental lead exposure which characterizes modern community life generally, outside the lead industries, no such accumulation occurs or it is so slight as to be insignificant in the course of a lifetime. This problem has been approached from several points of view. A few data that have been published previously are employed for illustration in table 5. The concentration of lead in the bones of persons of greatly differing ages at the time of death is shown. These cases were selected as carefully as possible to avoid the inclusion of any instance of occupational or other unusual lead exposure. One can make no claim for certainty in that regard, but for the sake of additional assurance, most of these data relate to women whose occupational histories were simple and apparently dependable. One sees that, despite the wide range of the life span, there is no consistent evidence of progressive accumulation of lead in the skeleton. One would anticipate that such evidence would most certainly show up in a series of this type. The defect in the more extensive and less critically chosen data that have been published in support of the existence of progressive accumulation of lead during

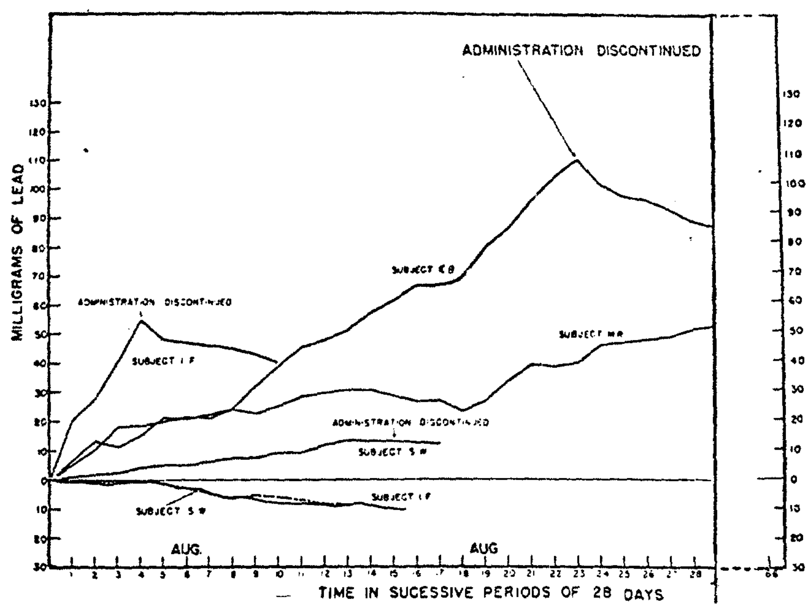

Chart 1.—Lead balance, retention and loss in normal adult human subjects under varying conditions of lead intake by ingestion. Points on the curves represent the cumulative total of the differences between the lead in duplicate samples of food and drink, plus that administered, and the lead output in the feces and the urine.

life can be appreciated, when one recognizes the great difficulty in the avoidance of persons who have been subjected to occupational or unusual types of lead exposure. Indeed our examination of Tompsett's data led us to suspect that some such unusual lead exposure had occurred in an appreciable number of his cases, a suspicion which was later confirmed by correspondence.

The next series of results illustrates a somewhat different approach to this problem. A series of curves is given in chart 1, each representing the facts in relation to one person studied under carefully controlled laboratory conditions. The intake and output of lead day by day over a period of weeks, months and years were determined by analytic means. The difference between intake and output has been plotted in each instance in a cumulative manner, so that the total quantity of lead retained in the body at any time, as the result of the experimental conditions, is indicated. These experiments are based on the most recent and most accurate methods used in the Kettering Laboratory for studying the alimentary and urinary metabolism of lead, that which is absorbed by way of the respiratory tract being ignored.

There are several points of interest in chart 1, to which I shall refer briefly. Two of the subjects (I. F. and S. W., represented in the lowermost curves) took a normal diet of their own choosing and no additional lead. It will be observed that these persons, in accordance with my previous statements, put out slightly more than they took in. The interpretation of this fact has been made before. The correspondence in the behavior of these subjects over a period of about eighteen months in each instance is so striking and so clearly defined as to be convincing. The discrepancy between the total intake represented by ingested lead in the food and beverages and the output in the feces and the urine approximated 10 mg. in the eighteen months. It is a minute quantity and you will recognize, in all likelihood, as I do, that no significant difference between intake and output could have been found from day to day. Prolonged observations were required to reveal the fact, but the trend continued in such uniform fashion as to be improbable of explanation as experimental error, and therefore it is accepted as fact.

Other curves in this series or family of curves illustrate the facts obtained in the study of other healthy human subjects under conditions of increased oral intake of soluble lead. The upper curve marked S. W. is that obtained in the case of a subject who took an additional 0.3 mg. of lead per day, as a solution of lead acetate, thereby bringing the total (including that in his food) to somewhat less than 0.6 mg. per day. At that level of intake the metabolism was not balanced, for some accumulation of lead occurred. The accumulation was slight, however, so that it is apparent that it will be difficult if not impossible, by these experimental means, to arrive at a level of daily ingested lead which is just at the point of balance with output. Clearly, the point of balance in experiments of this type is to be found somewhere between 0.3 and 0.6 mg. of lead ingested per day.

Another curve (M. R.) gives the facts on the retention of lead when 1 mg. of lead per day was added to the dietary lead. This curve with some vagaries continues substantially as a straight line for four and one-half years. Another (E. B.) illustrates the effects of the addition of 2 mg. of lead per day to the dietary lead. This curve continues straight or nearly so for two years. Another (I. F.) is the graphic result of the administration of 3 mg. per day, in addition to that in the diet. This experiment was terminated much sooner than it should have been, because of the fear, later found to be unwarranted, that the initial steep slope of the curve might be indicative of impending danger to the subject. It is apparent that over the periods represented in these observations the subjects failed to absorb quantities of lead which approach the point of saturation, so to speak, of the tissues in which lead is retained. Most of the retained lead found its way without undue delay into the skeleton, in which, obviously, the small quantities of lead were but traces in the bulk of minerals available. On this account, it is of the greatest physiologic significance to recognize that despite the substantially constant rate of absorption of lead from the alimentary tract in any individual experiment, there was a well defined progressive increase in the concentration of lead in the blood and the urine of every subject over the active period of administration of lead, with the single exception of the one whose lead intake was about 0.6 mg. per day. In view of the known facts concerning the distribution of lead in the tissues of the body over such periods of time, it is obvious that all or almost all of the lead absorbed into the tissues of these subjects, including that which found its way into their skeletons, exerted its effect in the maintenance of a state of dynamic equilibrium of the tissues with each other. Obviously little or none of the absorbed lead was stored in an inert form at any time, in the skeleton or elsewhere. In the case of the subject who ingested approximately 0.6 mg. per day for eighteen months, the total quantity of lead involved at any time during this entire period was too small to exert a demonstrable effect.

For practical purposes, these experiments demonstrate that the safe level for the ingestion of lead in food and drink, as determined by the establishment of a level of alimentary lead intake that will not result in the retention of lead on the part of normal healthy persons, is greater than 0.3 mg. and less than 0.6 mg. per day. It is fair to say that those of us who have interest in these matters in relation to the public health would like to see a situation maintained in which there is little likelihood of a practically significant amount of progressive accumulation of lead in the tissues of persons in the general population during their span of life.

INDUSTRIAL EXPOSURE TO LEAD

The foregoing facts and considerations have brought up the problem of industrial exposure to lead. It is clear that if the foregoing observations and concepts are valid, the degree of risk associated with occupational exposure to lead is the joint function of the severity of such exposure and its duration. The problem is to determine the limits of safe occupational exposure to lead, by providing criteria which can be applied pragmatically and by determining the physiologic facts concerning the relative importance of duration versus intensity of exposure under a variety of conditions. Fortunately, to a considerable degree these tasks are susceptible of accomplishment, and to a practical extent they have been accomplished.

As a background for this discussion, certain facts with respect to normal persons, unexposed to lead compounds during their day's work, must be reviewed briefly. At this point, it is necessary for me to say that Dr. Fairhall's[1] skepticism concerning the validity of the more carefully collected data on the concentration of lead in the blood of normal persons should not be permitted to obscure the facts. In presenting the data in table 6, candor requires me to point out that

TABLE 6.—*Mean Concentration of Lead in Blood of Persons and Groups of Persons with No Occupational Lead Exposure* *

Identification of Group or Person	Number of Persons or Samples	Lead, Mg. per 100 Gm. of Whole Blood
Mexican Indians	30	0.023
American students	30	0.027
Subject E. B.	9	0.029
Subject M. P.	6	0.038
Subject H. D.	76	0.034
Subject I. F.	37	0.031
Number of analyses	188	0.030
Probable error		±0.0005
Standard deviation		±0.009

* Range of analytic results: 0.005 to 0.055.

the background of experience and technical proficiency which has brought forth these results has been tested somewhat by time and by the critical investigation of others. I do not take credit for their accuracy, for they represent the work of colleagues who have labored with skill and assiduity to develop methods that would yield precise and final results. I have examined these results as to their precision and reproducibility with a critique for which I am responsible, and I am convinced that they will stand the test of time. A similar skepticism, now resolved, once attached to our results on the lead content of the urine of normal persons, as I remember.

It seems apparent, if you will accept these figures, that the concentration of lead in the blood of the present day normal person varies between the limits of 0.01 or slightly less and 0.055 mg. per hundred grams of whole blood, only an occasional sample exceeding the value of 0.05 mg. per hundred grams. It is also an important physiologic fact

1. Fairhall, L. T.: Analytic Methods in Diagnosis, Occup. Med. 3:13 (Jan.) 1947.

that from 95 to 98 per cent of this lead is found in the erythrocytes in the blood. This circumstance is responsible for the existence of a first line of defense on the part of the human organism against a high concentration of highly reactive lead in the medium bathing the cells of the body.

In table 7 are given the mean values of the concentrations of lead in the blood of groups of persons whose occupations involve varying

TABLE 7.—*Variation of the Mean Concentration of Lead in the Blood of Groups of Persons in Accordance with the Severity of Their Occupational Lead Exposure*

Occupation	Occupational Lead Exposure	Number of Persons in Group	Lead, Mg. per 100 Gm. of Whole Blood
Miscellaneous	None	188	0.030
Installing insulation	Hypothetic only	27	0.037
Garage mechanic	Very slight	145	0.039
Paint manufacturing	Well controlled	20	0.048
Soldering	Well controlled	15	0.050
Manufacturing of lead shot	Potentially hazardous	13	0.062
Color manufacturing	Hazardous	7	0.086
White lead manufacturing	Hazardous	21	0.086
Lead smelting	Highly hazardous	73	0.153

degrees of severity of lead exposure. The total range of such values as we have seen them is not covered by these data, but they serve to illustrate the important fact that increasing severity of exposure is associated with increasing concentration of lead in the blood.

TABLE 8.—*Concentration of Lead in Urine of Groups of Normal Adults with No Occupational Lead Exposure*

Lead, Mg. per Liter	Frequencies of Occurrence of Quantities of Lead Indicated			
	Americans	Mexicans	Frenchmen	Germans
0 - 0.009	..	5	..	..
0.01 - 0.019	7	10	11	5
0.02 - 0.029	6	7	6	4
0.03 - 0.039	8	4	8	2
0.04 - 0.049	5	3	5	1
0.05 - 0.059	3	..	2	1
0.06 - 0.069	1	..	1	..
Totals	30	29	33	13
Mean	0.029*	0.022	0.030	0.027
Probable error	±0.002	±0.002	±0.002	±0.002
Standard deviation	±0.016	±0.017	±0.014	±0.012

* The mean concentration of lead in the urine in nine hundred and forty-seven twenty-four hour samples of the urine of 4 normal American adults studied under carefully controlled laboratory conditions was 0.027 ± 0.0003 mg. per liter.

The range of concentration of lead in samples of large volume of the urine of normal persons is illustrated in table 8. Here it is of interest to see that the subjects include Americans, Mexicans, Frenchmen and Germans, among whom the distribution of the results is substantially the same.

Tables 9, 10 and 11 illustrate facts which are amply supported by large numbers of observations made over prolonged periods of time in certain lead industries, and over a wide variety of industries with variable degrees of hazardous exposure to lead. The analytic data refer to samples of large volume. It is apparent that the classification of occupational exposure to lead according to its severity by this means is readily made.

In table 9 the levels of concentration of lead in the urine that are compatible with complete freedom from the risk of lead poisoning are shown. The evidence behind this statement as well as others that

TABLE 9.—*Concentration of Lead in Urine of Persons with Safe Occupational Lead Exposure*

	Fequencies of Occurrence of the Quantities of Lead Indicated			
Lead, Mg. per Liter of Urine	Random Samples from Workmen, Industry E. P.	Repeated Samples from Nine Men, Industry D. P. L.	Repeated Samples from Subject M. R., on Experimental Intake of 1 Mg. Daily Plus That in Diet	Random Samples from Workmen, Industry H. R.
0.0 - 0.019	8	3	..	0
0.02 - 0.039	8	110	34	5
0.04 - 0.059	3	239	82	6
0.06 - 0.079	3	104	65	11
0.08 - 0.099	2	15	14	5
0.10 - 0.119	..	..	2	2
0.12 - 0.139	..	..	..	4
0.14 and over	..	..	..	3
Totals	24	471	197	36
Mean..................	0.037	0.051	0.057	0.079
Probable error.........	±0.004	±0.0005	±0.0009	±0.004
Standard deviation....	±0.025	±0.016	±0.013	±0.04

follow in similar vein is empiric, being based on careful clinical observations in a vain search for illness that could be regarded as relevant.

Table 10 presents data previously employed to designate the highest general level of urinary excretion of lead (as represented by large samples of urine) which, in our experience, was compatible with freedom from symptomatic plumbism. That is to say that men employed under conditions that gave rise to such levels of urinary excretion of lead remained free of symptoms and continued their work for years without complaint, illness or clinical evidence of plumbism. We were not sure in the past as to the margin of safety that was represented in this standard. As a consequence of experience during the war, when control of exposure was more difficult, we had the misfortune to establish the facts in this regard. Without going into details, suffice it to say that we have been conservative, without, I think, being overcautious, in the promulgation of this standard. Actually, the mean values, without great increase in the over-all range of values, can go to 0.11 mg. or 0.12 mg. without incidence of lead intoxication, but when an occupational group exceeds the latter value, evidence of lead intoxication can be found among them before long, in our experience. Our error, therefore, if it be called an error, was on the side of safety. In my opinion, after years of experience, the safety factor included in our original standard is not too great, when one considers that most occupations should be safe for an indefinite period of employment, rather than for a relatively short period of years.

TABLE 10.—*Concentration of Lead in Urine of Persons with Occupational Lead Exposure Maintained for Years Near Threshold of Toxicity*

Lead, Mg. per Liter of Urine	Frequencies of Occurrence of Quantities of Lead Indicated *
0.000 - 0.019	..
0.020	3
0.040	14
0.060	17
0.080	10
0.100	9
0.120	6
0.140	9
0.160	4
0.200	1
0.220	1
Total	74
Mean	0.097
Probable error	±0.004
Standard deviation	±0.045

* These data represent one set of results obtained on one large sample of the urine of each workman chosen to represent a specific occupation. The group as a whole represents all the occupations in a plant. Comparable results were obtained at intervals over a period of years. Decreases in environmental lead exposure resulted in elimination of some of the higher values and lowering of the mean; increases in exposure caused opposite effects. So long as there was no significant increase above the level illustrated here, no clinical plumbism was evident, but when higher individual values were obtained and mean values exceeded 0.12 mg. per liter, signs and symptoms appeared.

Table 11 illustrates the excretory values obtainable under occupational conditions which result in the occurrence of cases of lead poisoning. Cases increase in number and severity as the mean urinary concentration of lead increases.

I should like at this time to emphasize the fact that the order of magnitude of the exposure of individuals can be determined by analytic means in such a way as largely to dispose of the bugbear of individual susceptibility. We have learned that the variation in the response of individuals to the conditions of a lead trade is not due to the factor of susceptibility to lead so much as to the generally unrecognized variability of the lead exposure from person to person and from time to time in the same occupation. I do not mean that there is not biologic variation among workmen, but it operates within reasonable limits, and it definitely does not include the wide range of unpredictable susceptibility that is so commonly referred to in medical literature and comment. Our experience over a period of years has demonstrated clearly that if the lead exposure of a person is kept within certain reasonable limits he will not become ill. Admittedly, industrial employees are a somewhat selected group, and this, in itself, limits the factor of susceptibility, but within the limits of lead exposure which we have described as safe, individual susceptibility is not an important stumbling block to the accomplishment of satisfactory results.

TABLE 11.—*Concentration of Lead in the Urine of Persons with Demonstrably Dangerous Occupational Lead Exposure*

	Frequencies of Quantities of Lead Indicated		
Lead, Mg. per Liter of Urine	Random Samples from Workmen, Industry C. S. B.	Random Samples from Workmen, Industry B. B.	Random Samples from Workmen, Industry E. P.
0 - 0.07	11	4	6
0.08 - 0.15	31	27	28
0.16 - 0.23	14	17	20
0.24 - 0.31	8	7	13
0.32 - 0.39	2	1	3
0.40 - 0.47	1	2	5
....	....	....	....
0.48 - 0.55	1	..	4
0.56 - 0.63	..	2	3
0.64 - 0.71	..	..	2
0.72 - 0.79	..	..	1
0.80 - 0.87	1	1	..
0.88 - 0.95	1	..	..
0.96	3	1	1
Totals	73	62	86
Mean *	0.155	0.172	0.194
Probable error	±0.0071	±0.0075	±0.0079
Standard deviation	±0.087	±0.085	±0.102

* The mean has been calculated on results above the dotted line.

In response to a request and in consideration of a practical problem, it seems necessary to say something about the matter of "spot" samples of urine, versus samples of large volume, as a means of measuring the lead absorption of individuals or groups. In chart 2 are shown the results of three sets of observations made at three different periods in the history of a person exposed experimentally to a given amount of lead over a long period of time. The dotted lines represent the concentrations of lead in the blood on these occasions, while the solid lines represent the concentrations of lead in the urine. Observations were made at intervals of two hours during each of the three twenty-four hour periods. As can be seen, the concentration of lead in the blood is substantially constant throughout any one of the twenty-four hour periods, but it is higher at each successive period of the experiment, in response to the progressive retention of lead hitherto spoken of as occurring in such prolonged experiments. The variation in the concentration of lead in the urine on one of these days, which is the only present point of the demonstration, ranged from 0.07 mg. per liter at one time to a peak of 0.21 mg. per liter at a later time in the same day. This extreme degree of variation was a function of the volume of urine excreted at different times. When the volume was high, the urinary concentration was low, and vice versa. This illustrates the problem of sampling, so far as the physiologic principle is concerned. We have found it necessary to make use of spot samples under certain conditions, and such samples yield valuable information.

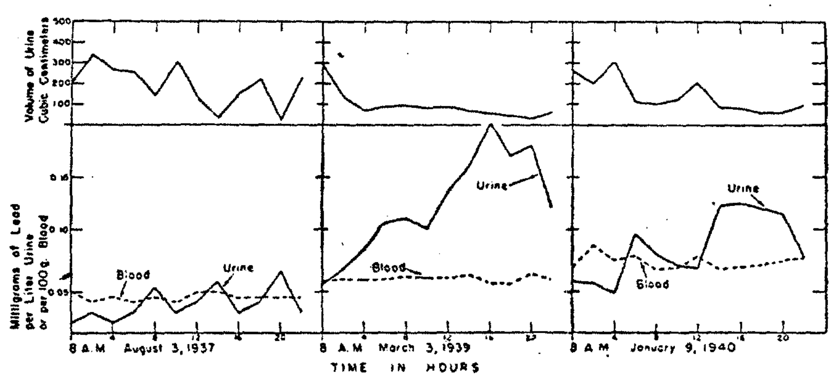

Chart 2.—Variations in concentration of lead in urine and blood during twenty-four hour periods (subject M. R.). The analytic results appearing as points on the lower section were obtained for the urine voided at two hour intervals and for samples of blood taken in duplicate at two hour intervals.

However, it is necessary to control the factor of diurnal variation. This can be accomplished in at least two ways, both of which are usually feasible. One consists in the determination of the specific gravity of the urine, making some allowance for the extent of the concentration of solids therein, while the other, more valuable, is that of taking a sample or samples of blood at the time the urine is collected, so as to be able to appraise the significance of the urinary concentration of lead on the background of the concentration of lead in the blood. By the combination of these procedures one is usually able to picture the physiologic situation, while at the same time one need not rely on one analytic determination. The advantages of this type of cross checking are great indeed, especially in medicolegal practice.

If one is studying a group of persons in a torrid climate and another in a cool one, one will find that the concentrations of lead representing tolerable conditions of lead exposure will be higher in the hot area than in the cool. Likewise there will be differences in the results obtained in the summer as compared with the winter, in temperate or semitropical areas. These factors have to be taken into account in the interpretation of results and in establishing standards of safety.

Another aspect of the problem of sampling is that of the contamination of samples in the process of their collection. This, above all factors, has contributed to the confusion which has tended to surround this subject. It is still not sufficiently well known that the handling of such samples by procedures that are customary and satisfactory in relation to many other analyses will result badly in almost every instance in the case of lead analysis. Blood must be collected in chemically clean containers, preferably of glass of extremely low lead content, and must be drawn through a needle that is fabricated and cleaned so as to be devoid of any lead. The brass hub which is a usual part of the structure of standard hypodermic needles will contaminate blood samples with lead and will give rise to high results. Moreover, the likelihood of contaminating samples of urine with dust or other foreign material is such that one must exercise the utmost care against contact of the hands or clothes of the individual with the sample. Personal advice and supervision is often required to avoid the mishandling of the stopper or cover of the container. Samples of blood, urine, spinal fluid or tissues collected for lead analysis in ordinary hospitals by ordinary orthodox methods are almost always seriously contaminated. It is this which has accounted for the publication of impossibly high results for the urine and of certain equally fantastic results for blood and tissues. When samples of urine exceed 0.6 mg. per liter in their reported lead content, it is well to ignore them unless the results are confirmed by the most careful technic. Except in the rarest instance of most unusually rapid absorption of lead, such results convict themselves of error. I have seen concentrations as high as 1.5 mg. per liter, but they are most rare, and concentrations of 2 mg. or more per liter are almost certainly incorrect.

THE DIAGNOSIS OF LEAD POISONING

I come now to the problem of diagnosis, with which, obviously, I cannot deal at this time in any satisfactory fashion. Most of what I have to say on this subject has been said in some detail and published where it is readily available. However, I want to make two comments. One of them is that the diagnosis of lead intoxication is made on presumptive or definite evidence of significant absorption of lead, together with the existence of a clinical syndrome which, when carefully studied by acceptable clinical methods, is found to be in keeping with the known toxic effects of lead on the human organism and is not more readily accounted for on the basis of other clinical considerations. My second comment, which to some degree is a corollary of the first, is that the known toxic effects of lead on the human organism are now susceptible of critical study and interpretation in a manner not previously possible. There is now available specific and fairly precise knowledge of the physiologic background by which one can estimate the significance of lead exposure and absorption. Persons do not get lead poisoning without having absorbed abnormal quantities of lead. When a person is suspected of having lead poisoning, it is well to establish that he has had a significant exposure to lead—not by his story or by casual observation of the conditions of his employment, but by physiologic means. The evidence, so far as it is entirely acceptable and not presumptive, resides in the man himself at the time of his illness, and can be obtained. It often becomes necessary in controversial and medicolegal cases to establish the order of magnitude of the exposure beyond presumption, and this can generally be done by suitable means. Such means should be used. Admittedly, such means call for difficult and precise procedures and unusual skill, as compared with most technics of the diagnostic laboratory. Thus there is a handicap to be overcome. Physicians have overcome handicaps in the past and they can overcome them in the future. Obviously, when the diagnosis cannot be proved by the most acceptable means, one must do the best that one can without proof. Such circumstances do not provide the proper basis for certainty, but they are often the background for dogmatic decisions. Unfortunately, medical procedure in relation to this problem is brought into disrepute by the exercise of arbitrary clinical judgments on the part of physicians who have not had or made use of the means of substantiating their opinions. It becomes increasingly important that physicians make use of the methods available for this purpose.

Printed and Published in the United States of America