Lead Absorption, Lead Excretion and Lead Poisoning

by

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The present problems in the differential diagnosis of lead poisoning, in so far as they differ from those of any previous period, arise largely in the evaluation of the significance of the lead exposure of a patient, and the interpretation of the meaning of such lead determinations as may have been carried out on the feces, urine, blood, spinal fluid, teeth, skin, or other tissues, in search of specific evidence of lead absorption. These problems, expressed somewhat differently, and considered from slightly different viewpoints, are among the most important practical questions in relation to plumbism, both in general medical practice and in industrial hygiene.

To the medical practitioner, the facts in the matter of lead exposure are often obscure. In the case of an

as a factor in illness until a chance x-ray plate shows suggestive or conclusive evidence of abnormal lead deposits in the skeleton. In the adult, industrial lead exposure may or may not be suggested by the occupational history. The absence or the occurrence of such suggestion may be equally misleading, since, on the one hand, lead exposure may exist in unsuspected occupations, while on the other, recognized lead trades may be so well regulated as to give rise to little or no exposure. Indeed technical and operating changes are carried out in modern plants with such disconcerting speed and frequency, that plant physicians themselves are not always conscious of their hygienic import. Obviously, the doctor who has no direct and detailed knowledge of plant activities and conditions, cannot be expected to place a proper value on the history of occupational lead exposure. In many instances, therefore, judgment requires that he base his opinion as to the severity of the exposure on specific evidences of lead absorption, rather than on non-specific clinical evidences of injury.

In the case of the industrial physician, the significance of the lead exposure in a plant can become partially known, in time, through its clinical effects upon the plant population, but it cannot be anticipated or properly appreciated without recourse to some precise means for measuring either the magnitude of the potential exposure, or, preferably, the physiological response to exposure in terms of the lead absorption and lead excretion of the workmen.

Even with the necessary facts available as to the nature and magnitude of the lead exposure, an interpretation of their clinical significance may still be difficult, particularly if the exposure is known to be slight. The reputation of lead as

an insidious poison the minutest quantities of which, if absorbed repeatedly over a prolonged period, might accumulate in the body with disastrous results, has long been established both in the medical and the lay mind. Gradually physicians with experience in the lead trades, who noted the results of various types and degrees of lead exposure, came to believe that lead absorption did not cause injurious effects if it did not exceed certain limits. The original distinction between dangerous and essentially harmless occupational lead exposure was based on observations of workers and plants, without benefit of quantitative methods of study. With the recognition of the greater significance of inhaled lead as compared with ingested lead and with the development of satisfactory methods for the estimation of particulate lead in the air breathed by workmen, the existence of a threshold value for toxic lead absorption has apparently been established. However, many physicians, physiologists and pharmacologists have either disregarded the observations made in this field or have considered them with suspicion and skepticism. Only recently has evidence been obtained from the study of human lead absorption and excretion under a variety of conditions, which substantiates the position taken by the industrial hygienist. Because the meaning of this evidence has not been fully appreciated, it seems well to outline it here, not only in relation to lead absorption on the part of the general population and to the diagnosis of lead poisoning in the hands of the average clinician, but also as a basis, in principle, for industrial practice.

The presence of lead in the tissues and in the excreta of normal individuals, quite apart from any occupational exposure to lead compounds, is now established. In 1933, we

reported in detail the data of our studies up to that time and reviewed the observations of other workers (1, 2, 3). Since the publication of these reports, many additional contributions have demonstrated the occurrence of lead in the skeleton (including the teeth) (4, 5, 6, 7, 8, 9, 10, 11), the soft tissues (7, 9, 11, 12, 13, 14, 15) (including the brain (9) and the cerebro-spinal fluid (16, 17), the blood (18, 19, 20, 21, 22(a)) urine (9, 18, 20, 22(b), 23, 24, 25, 26, 27, 28) and feces (20, 26) of normal persons of all ages and occupations. An examination of the results obtained by different analysts in various parts of the world shows them to be in remarkably close agreement, with due allowance for variations in the sensitivity and accuracy of the analytical methods employed. The general pattern of normal lead metabolism which we have described in relation to the American population seems to have been confirmed, not only in the American environment but in the several countries in which similar observations have been made. Of particular interest to us in this connection are the results obtained by Lynch and his associates (8) on the lead content of the bones of presumably normal persons (Great Britain), and those of Tompsett and Anderson (9), and Tompsett (10) on the lead content of the skeleton and soft tissues of human fetuses and human beings of widely varied ages (Great Britain). These data would seem to show that the lead content of the tissues of a normal child and of a normal adult as reported by us (2), was of an order of magnitude fairly characteristic of normal human beings in general. We are justified, therefore, in making a confident restatement of the facts with regard to normal human lead metabolism in their simplest

terms. The adult American ingests lead in his food and drink to the extent of approximately 0.25 milligrams per average day (20) (He probably inhales a small quantity of lead from the air he breathes (29, 30, 31, 32, 33, 34, 35), although the amount inhaled and the proportion absorbed from that which is inhaled are conjectural.) Most of the ingested lead traverses the alimentary tract unabsorbed, but some quantity is absorbed as is shown by the constant presence of lead in the tissues, the blood, and the urine. The mean daily fecal output of lead is approximately 0.25 milligrams (20), while the daily urinary output varies from 0.02 milligrams to 0.10 milligrams (20, 26), the variation being chiefly related to weather conditions with their attendant influence upon urinary volume (26). The lead of the tissues is distributed in accordance with a definite pattern, with the major portion in the skeleton (and apparently with a higher concentration in such long bones as the femur (5, 10), but with measurable and apparently fairly constant quantities in the soft tissues, especially in such as the liver, kidney, spleen and brain (2, 9). The average gross quantity present in the adult body is somewhat in doubt, because of the paucity of data, but it is probably not less than 100 mg. nor more than 200 mg. with due regard to variations in body weight (2,5,9,10,36). Barth (36) supplied data which in his opinion pointed to a progressive elevation of the lead concentration of the skeleton with progressing age. However the differences between youth and old age were too slight and too irregular to be convincing. Tompsett (10) found similar and even larger variations in different bones of the same skeleton and in the skeletons of different persons within the same age group. The combined facts furnished by the study of the tissues and excreta indicate that within certain limits of intake, a state of dynamic equilibrium

is maintained in which progressive lead accumulation in the tissues does not occur, intake and output having come into balance after a certain level of absorption has been reached. Significant variations in absorption and excretion occur from day to day, but the normal metabolism of lead, as compared with that of the more common metallic constituents of living material, is remarkably stabile. Whether or not lead is useful in physiological mechanisms is an open question at present, but regardless of the eventual answer to this question, the concept of lead as an accumulative poison, without regard to quantity, has received its death blow.

Elsewhere, we have interpreted the foregoing facts in their relation to the diagnosis of lead poisoning (37, 38). It is not our purpose here, therefore, to give further detailed consideration to this aspect of the subject. We merely wish to stress the necessity for taking strict account of the limits of normal variation in the clinical interpretation of data on the lead content of the tissues or the excreta of patients. In view of present knowledge of the normal picture and of deviation induced by abnormal exposure to lead compounds, lead analyses of various types take their place as invaluable diagnostic aids, and as useful clinical and medico-legal evidence. However, such procedures become useless and even grossly misleading unless they are carried out with precision and interpreted with due regard for the available knowledge as to the behavior of lead. Moreover, analytical data cannot be substituted for sound clinical observations in any of the fields in which they have come to be useful adjuncts.

The ultimate sources of the lead which is found in human food merits further consideration and further detailed study. As we have pointed out previously (39), the increment of lead

content above that which is a normal constituent of our food substances, is due to contamination from a great variety of sources, some of which are of recent and some of earlier origin. A number of the earlier sources of contamination of food and drink have disappeared, some by accident and others by intent. Our data on the fecal lead output of normal persons in various parts of the United States and Canada, as collected over a period of more than a decade, do not give evidence of a tendency toward a progressive increase in dietary lead. This is not to imply that our sampling of the population has been such as to yield adequate information on the extent or the causes of variation in these respects. Nevertheless we have been struck by the essential uniformity of the data obtained from year to year, and we doubt the occurrence of any recent progressive increase in the lead intake of the American population. We do not suggest, however, any over-confident relaxation of the efforts being made by those engaged in the supervision, handling, and processing of our food materials, to prevent contamination with lead.

An ultimate basis for determining the limits of safety in the matter of lead absorption, in both the general and the industrial population, can be found only in further experimental studies of the fate of lead when introduced into the human body through various avenues of entrance. We have illustrated certain abnormalities in the lead content of the tissues and excreta of persons exposed to abnormal quantities of lead both of occupational and non-occupational origin (40). In observations made chiefly in various lead trades, we found a correlation between the rate of lead excretion and the severity of lead exposure. The available data appeared to indicate that within certain limits of increasing

exposure and presumable absorption, there was a proportional increase in the urinary excretion; with further increases in exposu there was a progressively diminishing increment of increase in the excretory response. There was also an incompletely defined relationship between the magnitude of the lead exposure, as portrayed by rate of lead excretion, and the occurrence of lead intoxication among the workmen. We came to the conclusion, which Shiels (41) has since reached from his observations, that lead poisoning may be expected to occur under occupational conditions in which lead is excreted by representative workmen at a mean rate above 0.21 mg. per liter in the urine. In subsequent plant studies we have kept in mind the need for defining more precisely in terms of lead excretion, the highest level of lead exposure compatible with complete freedom from clinical lead intoxication. As evidence of some progress toward this goal, the following recent observations are reported. *

Groups of men, selected as representative of the various occupations in three different industries, were examined by methods which we have detailed previously (42). Various samples of blood, urine and feces, as indicated in the data, were obtained with suitable precautions against contamination. The work of each group involved exposure only to particulate inorganic lead compounds. The men in Group A, all engaged in the same general type of work, handled a finished material which contained lead in an essentially insoluble form in a siliceous base. The conditions of

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* The full data of these studies will be given elsewhere. Brevity necessitates use of only those items of information and data which illustrate the points under discussion here.

exposure were not thought to be such as to permit absorption of lead to more than a theoretical extent. The men in Group B were employed in various types of soldering activities, but all had the same type, and apparently about the same degree of exposure to fumes of molten lead and to finely divided metallic lead and lead oxide. The men in Group C were likewise exposed only to fumes and to particulate lead resulting from varied types of operations with molten lead and lead castings. However the operations in this plant, as represented by this small group of workmen, involved somewhat variable degrees of lead exposure of a generally greater severity than that of the other plants.

The clinical data on groups A and B were entirely devoid of evidences of lead absorption or lead intoxication. In the case of Group C, however, certain individuals were seen to have absorbed lead in sufficient quantity to produce slight but definite gingival blue lines, characteristic changes in the blood picture, and slight but unmistakable evidences of neuro-muscular damage. In addition to these objective findings there were scattered but suggestive evidences of minor toxic effects in the form of vague gastro-intestinal complaints. One typical history of a recent episode of saturnine colic was obtained. No history of fatal or permanently disabling plumbism could be elicited from management, plant physician, or employees over the period of their direct knowledge and experience. Improvements in ventilation had been made some two years previously, since which time cases or suspected cases of incipient intoxication had been cared for either by temporary cessation of employment or more frequently by transfer to work involving less exposure.

The age distribution of the men selected to represent the various occupations in each industry, as given in Table 1, is of interest only because it demonstrates the representation of widely divergent age groups. The duration of continuous exposure, shown in Table 2, is correspondingly representativ of both short and long periods, except in the case of Group A in whi the longest period of employment coincided with the life span of the industry up to the time of our observations. The data in Tables 3 and 4 on the fecal output of lead, (results were not available for Group A), should be interpreted in relation to our previous demonstration of the role of alimentary lead as an approximate measure of the magnitude of exposure in dusty lead trades. The difference between the results obtained in the two groups is not significant, statistically, on the basis of comparison of the mean values for lead found in a single fecal evacuation. However, the two groups are significantly different with respect to alimentary output when compared as to their mean lead output per gram of fecal ash. This indicates that the exposure of Group C to particulate lead in the atmosphere was greater than that of Group B. Both mean values are above mean normal levels.

The results on the urine (Table 5) are much more significant than those on the feces, both in their general physiological meaning and in the clarity with which they portray differences in the lead absorption of the three groups of workmen. The mean rate of urinary excretion for Group A is within normal limits, as was expected; that for Group B is higher, and that for Group C is still higher, both differences being of statistically significant proportions. Thus the analytical results on the excreta correspond to the observed conditions in the plant, and

verify the existence of three different levels of lead exposure and absorption. *

It is a matter of both scientific and practical importance that the results obtained on samples of blood (Table 6) from workmen in Groups A and B do not differentiate these two groups with respect to their absorption of lead. It is probable that a differentiation would have been effected if a larger number of blood samples from Group B had been analyzed. Furthermore three analyses on blood from individuals in Group C, yielding 0.09 mg., 0.23 mg., and 0.49 mg. per 100 grams of blood, leave little doubt as to the status of the group in this respect. Nevertheless, the fact remains that with due regard to the numbers of samples available for analysis, the results on the blood do not yield as definite evidence as those on the urine, with respect to the conditions under study. (The mean value of 0.078 ± 0.007 for the urinary results which correspond to the fourteen analyses on the blood in Group B is significantly greater than the mean for Group A.) The reason for this can be found, we believe, in physiological considerations. Urinary lead excretion varies from person to person and in the same persons with a variety of individua

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* Determinations of the particulate lead in the atmosphere of Plant B, as carried out with standard methods by other observers at a somewhat earlier date, provide useful correlative data. The observe lead concentrations ranged from 0.033 mg. Pb up to 0.63 mg. Pb per cubic meter of air, with a mean value of 0.21 ± 0.02 mg. Pb per cubi meter in thirty-one air samples taken from various parts of the plan

and environmental factors. However, the concentration of lead in a sample of urine collected over a period of twenty-four to seventy-two hours, in accordance with our practice, shows some degree of response to all the physiological factors active during that period, including variations in lead absorption. A single blood sample, on the contrary, illustrates only a momentary physiological state, which, under essentially constant conditions of lead exposure, may conceivably represent the general level of the lead metabolism more adequately than a sample of urine, but which under conditions of variable or intermittent exposure could scarcely be expected to do so.

The clinical and analytical data as a whole do not justify sweeping conclusions. Further study of these industries and of others with different basic levels of lead exposure will be required to define, in terms of lead metabolism, the upper level of lead exposure which is compatible with human safety. However these observations represent another step toward that goal.

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TABLE I

Distribution of Persons Employed in Three Lead Industries According to Age

Age In Years	Frequency		
	In Industry A	In Industry B	In Industry C
20 - 24	2	3	4
25 - 29	9	2	2
30 - 34	5	3	
35 - 39	4	6	3
40 - 44	2	8	10
45 - 49	2	4	2
50 - 54	3		1
55 - 59		3	
60 or more		7	
Total	27	36	22

Table 2

Distribution of Persons Employed in Three Lead Industries According to Duration of Continuous Exposure in Same Plant

Period of Exposure in Years	Frequency		
	In Industry A	In Industry B	In Industry C
Under 1.0	8		
1.0 - 2.9	15	6	9
3.0 - 4.9	4	6	
5.0 - 6.9		4	3
7.0 - 8.9		4	5
9.0 - 10.9		7	1
11.0 - 12.9		3	
13.0 - 14.9		1	3
15.0 or more		5	1
Total	27	36	22

Table 5

Distribution of Persons Employed in Two Lead Industries According to Lead in Single Fecal Evacuation

Lead in Milligrams per Sample	Frequency	
	In Industry B	In Industry C
0 - 0.149	4	4
0.15 - 0.299	7	5
0.30 - 0.449	8	5
0.45 - 0.599	4	5
0.60 - 0.749	2	4
0.75 - 0.899	2	6
0.90 - 1.049	3	2
1.05 and over	3	4
Total	33	35

Mean	0.457 ± 0.037	0.619 ± 0.053
Standard Deviation	± 0.304	± 0.435

TABLE 4

Distribution of Persons Employed in Two Lead Industries According to Lead per Gram of Ash in Feces

Lead in Milligrams per Gram of Ash	Frequency	
	In Industry B	In Industry C
0 - 0.049	3	1
0.05 - 0.099	14	6
0.10 - 0.149	7	8
0.15 - 0.199	2	7
0.20 - 0.249	4	7
0.25 and over	3	6
Total	33	35
Mean	0.125 ± 0.010	0.164 ± 0.011
Standard Deviation	± 0.083	± 0.097

TABLE 5

Distribution of Persons Employed in Three Lead Industries According to Concentration of Lead in Urine

Lead in Milligrams per Liter	Frequency		
	In Industry A	In Industry B	In Industry C
0 - 0.049	17	10	
0.05 - 0.099	6	15	6
0.10 - 0.149		9	9
0.15 - 0.199			10
0.20 - 0.249			8
0.25 - 0.299			3
0.30 - 0.349			2
0.35 and over			3
Total	23	34	41
Mean	0.037 ± 0.004	0.081 ± 0.004	0.181 ± 0.013
Standard Deviation	± 0.025	± 0.036	± 0.121