Lead Absorption Versus Lead Poisoning

by

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Despite the availability of sound and well established methods for recognizing and preventing dangerous occupational lead exposure, there is still an unnecessarily high incidence of lead poisoning among industrial workers. Moreover, despite the existence of generally reliable diagnostic criteria, a surprising degree of confusion and uncertainty often enters into the consideration of a suspected case of plumbism whether the question at issue is the proper care of a sick man, the hygienic status of a plant, the granting of compensation, or the outcome of litigation. For these reasons one may be justified in restating certain facts which seem to require emphasis, as a background for a practical discussion of certain methods of procedure and their significance in industrial hygiene.

The Character and Significance of Normal Lead Metabolism

It would seem almost a platitude now to state, as we were criticized for doing in 1933, that "the presence of lead in human excreta and human tissues, as well as in living organisms in general, is an inevitable consequence of life on a lead-bearing planet". Without citing the extensive evidence in support of this statement, therefore, let us review the facts in so far as they concern the average normal healthy American adult. He ingests with his daily food and drink quantities of lead varying from 0.05 mgm., rarely, to somewhat more than 2.00 mgm, occasionally, the mean quantity over a period of months being approximately 0.33 mgm. He takes into his body by inhalation with the air he breathes a small and relatively insignificant quantity, which probably rarely exceeds 0.10 mgm per 24 hours, and of which only a portion- doubtless a variable but otherwise unpredictable portion -, is retained by the respiratory membranes and eventually absorbed into the tissues, the remainder being either exhaled or trapped in the upper respiratory tract and subsequently swallowed. (The quantity absorbed is so small as not to be apparent in prolonged studies in which the total lead output is balanced against lead intake by ingestion only. Considering the promptness and the magnitude of excretory response under conditions of occupational lead absorption from inhalation, one may conclude that under average normal conditions this type of lead absorption is indeed minute.) Little ingested lead is actually absorbed into the body. A very large proportion of it traverses the alimentary tract unabsorbed and appears in the feces. Some portion is absorbed and carried to the liver, is partly excreted with the bile back into the alimentary tract, and is soon lost from the body with the feces. The result of these and perhaps other avenues of secretion into the alimentary tract is to make the daily fecal lead output almost

(Slide 1) equivalent to the total intake by ingestion. Some small quantity escapes removal by the liver and is carried in the blood from which it is lost both to the tissues and to the excretions. Recent observations would seem to show that the blood is in equilibrium with the tissues of the body as a whole, with respect to its lead content. In any case lead is constantly found in the

(Slides 2 and 3) blood and in the urine in quantities subject to but minor variation. Thus the whole blood of normal healthy American adults usually contains from 0.01 mgm to 0.05 mgm per 100 grams, with a mean value of approximately 0.03 mgm per 100 grams. (Concentrations as high as 0.07 mgm per 100 grams are occasionally found). Very little of this is in the plasma, 95 per cent or more being found in the cells, mainly, presumably, in the erythrocytes. Lead is

(Slide 4) found normally in the urine in quantities varying from 0.01 mgm

" 5) to 0.08 mgm per liter with a mean value slightly in excess of

" 6) 0.03 mgm per liter. The mean urinary lead concentration may be seen to approximate one tenth of that in the blood. The lead in the tissues ~~is~~ distributed in accordance with a definite pattern, with the major portion in the skeleton and with a higher concentration in such long bones as the femur, but with measureable and fairly constant quantities in the other tissues among which the liver, kidney, spleen and brain are especially noteworthy.

Slide 7) The average gross quantity of lead present in the body of the

" 8) normal human adult is somewhat in doubt, because of the scarcity

" 9) of data, but it is probably not less than 100 mg. nor more than three to four times this quantity, with due regard to variations in body weight. Barth believed his data on the skeletal lead content pointed to a progressive increase in the concentrations with age, but the differences in youth and old age were too slight and too irregular to be convincing. Calvery has drawn the unwarranted conclusion that Tompsett's results on the lead concentration in various parts of the human skeleton (Scotland) demonstrate a progressive accumulation throughout human life. There is admittedly a statistically significant degree of positive correlation between the ages and the lead concentrations in the femur and the tibia of Tompsett's cases, but there are almost as large variations within narrow age groups as can be found in relation to extremes of age. Moreover, Calvery's assumption that the tissues of persons with significant occupational or incidental lead exposure shortly before death has not been included in these analyses is justified neither by Tompsett's statements nor his data. One may properly suspect, therefore, that variable environmental factors (dietary and otherwise), with variable individual lead intake, serve better to explain differences between normal individuals with respect to the lead content of their bodies, than can the variability in the duration of an essentially common and constant lead intake. The indirect evidence against the indefinitely progressive accumulation of lead in the tissues of persons exposed to fairly constant environmental conditions is much too great to be ignored.

It has been demonstrated clearly that the urinary lead excretion of individuals and of groups of persons varies with the magnitude of their current lead absorption, and that an abrupt change in the level of lead intake results in a
(Slide 10) fairly prompt excretory response. Recent observations show
(" 11) that this response to a known and constant magnitude of increased lead intake is not immediately maximal, but that it gradually builds up to a level which is dependent primarily upon the quantity of lead which has been <u>absorbed and retained</u> in the body. Within the limits which have been studied it does not continue indefinitely to increase but reaches a level which is maintained so long as the lead intake remains at a constant level. These facts are in complete harmony with the information
(Slide 12) obtained on groups of workmen with prolonged exposure to fairly constant and apparently safe occupational conditions. The urinary lead excretion of representative workmen clearly defines the magnitude of the lead exposure not only of an industry as a whole, but of characteristic and well isolated occupational groups within the industry. Moreover, the group levels of urinary lead
(Slide 13) excretion ~~do not~~ increase progressively but remain substantially
" 14) constant over long periods of time (years) during which little or no change occurs in plant conditions. Such observations combined with the facts obtained in the study of single individuals can hardly be explained except on the basis that the rate of urinary lead excretion is determined chiefly by the gross lead content of the body as an organic whole, and that the maintenance of a constant or nearly constant rate of urinary lead excretion is evidence of an

essentially constant quantity of lead in the body. There is adequate factual background, therefore, for the concept that within certain limits of lead intake, a state of dynamic equilibrium is maintained within the human body whereby lead intake and output are balanced over long periods of time, and progressive accumulation in the tissues does not occur.

The importance of the considerations outlined in some detail in the foregoing paragraphs cannot be overemphasized in their relation to the problems of public and industrial hygiene that arise from the use of lead compounds. Since lead is an inevitable constituent of human tissues and excretions, it is quite obvious that there are certain normal and physiological mechanisms into which this element enters whether incidentally or usefully. There can be no doubt that lead can be introduced into the human body without prejudice to the normal health and development of the organism, and that a toxic effect on the part of this element as well as of many others is a matter of concentration. The degree of control of public and industrial lead exposure which is necessary to avoid human hazard, therefore, is not to be determined on the basis of the pragmatic avoidance of the worst effects of the absorption of an intrinsically poisonous element, but on precise information as to the limits of lead exposure and absorption which are unattended by any toxic manifestations, or, which, in other words, are physiological.

The Evidences of Occupational Lead Absorption.

The existence of occupational lead exposure can usually be recognized by a survey of the materials and activities in an industrial plant. The general order of magnitude of the exposure can be estimated by the determination of the lead content of the atmosphere of working spaces, by the use of methods which have been so well described and are so satisfactory for their purpose that they need not be given more than passing mention here. One must emphasize the fact that through their adequate and consistent use, it is possible to determine the degree of the occupational hazard and the extent of the need for preventive and precautionary measures. Indeed if the lead content of the atmosphere of workrooms in the lead trades generally were maintained within the limits now recognized as safe in practice, occupational saturnism, from any other than accidents in plant operations, would cease to occur. However, so long as the hazards of many plants are not under such control, and so long as opportunities for accidental and inadvertent lead exposure exist in industry, it will be necessary to provide medical supervision which will be on the alert for the earliest signs of potentially dangerous lead absorption. The physiological evidences of lead absorption above the normal level should be clearly understood, [illegible]

[illegible]

[illegible]. It should also be recognized, as it not always is, that such evidences do not necessarily signify existing or impending lead intoxication. Lead absorption is not synonomous with lead poisoning. The absorption and excretion of quantities of lead considerably in excess of the usual and normal levels is wholly compatible with normal and healthy human life and activity, and if certain limits are not exceeded, no intoxication is to be anticipated.

The earliest sign of elevated lead absorption, and one which fortunately, is specific for lead alone, is found in an increased rate of urinary lead excretion. The demonstration of a small increase requires careful procedures for the collection of samples and some detailed knowledge of the physiological factors concerned with the urinary excretion of lead. Various published statements have appeared to the effect that the urinary lead fails frequently to reveal the extent of lead absorption, that the results obtained on urine samples are too variable and that the blood, more constant as to its lead content, should be used for obtaining analytical information. These conclusions have sprung from inexperience or from the use of inadequate methods for the collection and analysis of samples. It is true that urinary samples of small volume obtained at random are subject to considerable variation in their lead content. In individual cases, the latter varies chiefly with the water output of the period of their collection, i.e. if the urine is concentrated the lead concentration is relatively high, if dilute from high water intake or diuresis the lead concentration is relatively low. This factor can be controlled, in the case of small volumes, by proper selection of the time of sampling so as to avoid extremes of water intake and output; it can be eliminated altogether by collecting several liters of urine, making sure that no unusual quantities of liquid are taken to speed up the collection of the sample. Equally important is the avoidance of contamination of urinary samples, and the smaller the sample the greater must be the care in this respect. Urine samples collected in the usual types of washrooms or medical quarters in manufacturing plants, or obtained by customary hospital procedures, or, in fact, secured by any other than by precise methods controlled by the examiner, are not only valueless but grossly misleading as to their lead content. Lead is ubiquitous, and it is difficult under the most favorable circumstances to avoid all sources of contamination. Numerous case reports in current journals include analytical data on the urine which by mere inspection can be discarded as erroneous. In some instances the quantities found bear no relation to the conditions of exposure known or believed to have existed, and in others they are entirely beyond the maximal limits of urinary lead excretion. In this connection it should be pointed out that a urinary lead concentration in excess of 0.5 mgm per liter is a very great rarity, that concentrations higher than 0.3 mgm per liter are associated only with grossly dangerous conditions of lead exposure and absorption, while values exceeding 0.20 mgm per liter cannot occur without a definite and significant exposure to lead such as is associated with the admittedly hazardous lead trades. Prolonged exposure in doubtfully hazardous occupations has not, in our experience, induced such rates of urinary lead excretion.

In the foregoing discussion, the dependence on results expressed in terms of urinary lead concentration rather than on the basis of lead output per unit of time comes from certain practical advantages and experimental necessities. The urinary lead concentration can always be determined but measurements of the excretory rate in the time sense is not always feasible. Moreover, the urinary concentration of lead now has a physiological significance which is more certain than is that of the lead output per day. For comparative purposes, therefore, analytical results should always be expressed in terms of concentration, and, if possible, on a time basis as well.

The greater stability of the blood, with
Slide 15 respect to its lead concentration, from hour to hour, as compared
" 16
" 17 to the urine, is unquestioned. On the other hand the change in
" 18 the blood concentration as a response to lead absorption is
proportionately less than that of the urine, the result being that the effects of exposure are more easily demonstrated by the urinary lead concentration than by that of the blood. The chief advantage of the analysis of the blood, for diagnostic purposes, lies in the fact that it requires no manipulation on the part of
Slide 19 the person examined. If proper precautions are taken by the examiner, therefore, no factor of contamination need be considered. Blood samples, however, must be taken with the utmost precaution in a dust-free room, by means of specially fabricated needles, into specially cleaned containers. The minutest details of handling are of the same importance, though of different type, as those used in the maintenance of aseptic technique in surgery. Lead, like minute living organisms, enters into samples through the air and by means of contact with any save the most meticulously purified water, reagents, glassware and other equipment.

The significance of the fecal lead content in relation to lead exposure and absorption has been amply presented elsewhere and need not be discussed here.

Other signs of lead absorption above normal levels are (1) changes in the quantity and distribution of basophilic material within the erythrocytes and (2) the appearance of punctate deposits of lead sulphide in certain mucous membranes, especially in the margin of the gum tissue. Neither of these signs, contrary to opinions and written statements of many, is indicative of lead intoxication. Both occur in entirely healthy persons, except that the lead line does not appear without bacterial invasion of the gingival tissues, i.e. some degree of gingivitis is necessary for its development.

Punctate basophilia, or "stippling" of the erythrocytes, within certain limits, is of normal occurrence in the human blood. In examining the blood of some thousands of apparently normal healthy adults free of occupational lead exposure, we have found such erythrocytes in numbers ranging from one or two up to as high as six thousand per million erythrocytes. Some 6 per cent of the group showed one thousand or more per million erythrocytes, while the mean figure for 754 persons was 339.18 ± 9.72 per million erythrocytes. The number of such stippled erythrocytes in the blood shows little or no change with small increments of increased lead intake, but at higher levels of exposure and absorption their number in the circulating blood tends to increase. Considerable variation in the degree of individual response is observed, and fairly wide variations occur from day to day, but with increasingly severe conditions of lead exposure there is a definite trend toward increasing numbers of stippled erythrocytes in the blood of exposed workmen, if comparisons are based on groups rather than individual reactions.

These facts are responsible both for the usefulness of regular microscopic examinations of the blood of workmen as a means of estimating the significance of their occupational lead exposure, and for the inadequacies of such measures for diagnostic purposes in individual cases. Suffice it, in this necessarily limited discussion, to point out, that hazardous exposure to lead compounds is associated with the appearance of definitely abnormal numbers of basophilic erythrocytes in the blood of a considerable proportion of exposed workmen, while the absence of such erythrocytes in a suspected or alleged case of lead poisoning, during the period of active intoxication, is very nearly conclusive evidence that the toxemia is due to some factor other than lead.

A "lead line" may appear in gum margins which are somewhat inflammed by bacterial invasion whenever the lead content of the involved tissues is sufficiently elevated. We have observed the appearance of a faint blue line in an infected gum pocket in one person whose blood contained lead to the extent of 0.05 mgm per 100 grams. There is little doubt that easily identified lead lines signify somewhat higher levels of lead absorption. Nevertheless obvious deposits of lead sulphide are seen in the gums of persons with no demonstrable symptoms or signs of intoxication. They must be differentiated from similar deposits resulting from the precipitation of other metallic sulphides, notably of bismuth, and they must not be confused with the normal pigment of negroes and correspondingly dark-skinned peoples. The former differentiation is sometimes provided by the medical history of the person in question, but may require analyses of the blood or urine or both; the latter can usually be made by careful study of the locus and appearance of the pigment. The natural pigment is rarely, if ever, found in the gum tissue on the lingual side, while, despite the scant attention given the fact by clinicians in general, a favored site for the first appearance of lead line is in the extreme lingual edge of the gum opposite the bicuspids and lower molars. The bluish-purple line of gingival congestion may be taken for lead line by the inexperienced, and especially if no examination is made after expression of the blood by means of a transparent applicator (such as a glass slide). More commonly, the stained or discolored surface of a tooth just visible beneath a thin layer of gum tissue is called a lead line. The differentiation is not always easy and resort must sometimes be had to the use of a hand lens, or even to biopsy followed by microchemical or better by spectrographic analysis.

The Recognition of Dangerous Lead Exposure

Time does not permit a useful or adequate description of the symptoms and clinical signs of toxic lead absorption, nor is it my purpose to do more than to stress the necessity for basing the recognition of such absorption on the actual occurrence of illness which is compatible with the known clinical picture of saturnism, or upon sequellae which can at least be attributed plausibly to the effects of such absorption. It will be objected that this point of view leaves the matter to the judgment of the clinician and takes it out of the realm of conclusions which can be reached by methods and instruments of scientific precision. One can only answer this objection by reminding the properly enthusiastic proponents of laboratory methods in industrial hygiene, that their most significant function is to chart the conditions under which illness is likely to develop and to point the way for the identification of such conditions. The demonstration of signs of lead absorption above the normal level constitutes a useful exercise of this function. The actual recognition and identification of illness is a function largely and logically reserved to the physician. One may confidently anticipate that the further correlation of the signs of lead absorption with detailed clinical data on the types of toxic response and their frequencies of occurrence, will delineate dangerous lead exposure in quantitative terms so explicit as to compel its recognition and elimination.