

July 22, 1964

Dr. John H. Ludwig, Chairman
Working Group on Lead Contamination
Department of Health, Education and Welfare
Robert A. Taft Sanitary Engineering Center
4676 Columbia Parkway
Cincinnati, Ohio (45226)

Dear John:

I hasten to discuss Dr. Goldsmith's editorial suggestions with him and you, before it is too late (I am leaving for my vacation on July 31 to be gone until September 2). In doing so I am not attempting to retain what has been written, without change, but rather to avoid speculation and controversy in a part of the report which should be, so far as possible, a simple statement of the facts.

With reference to John's comments about the fate of the lead alkyls in the body, and the possibility (which is not that, but is rather a certainty) that their metabolism in the body and their distribution in the tissues differ from that of the inorganic compounds of lead, I have this to say. While a great deal is known about the initial and ultimate distribution of the alkyl lead compounds in the tissues, it is irrelevant to this discussion. While we have left the quantitative representation of the alkyls in the ambient air somewhat open to question, we have shown, by the data in this report, that the quantities are small to the point of practical insignificance, as a factor in the exposure to lead to which the general population is subjected. There is, therefore, no virtue, in raising this issue in this report, beyond the treatment that has been given to it, and certainly it would be a source of ambiguity in the discussion on page 20.

In order to emphasize the foregoing point still further, let me say that the last five lines of John's statement in the second paragraph of his letter should be deleted in any case, for they suggest that there is little or no information on the points raised. The facts are otherwise. A fair sized population of men have been engaged in the manufacture of tetraethyllead for many years (tetraethyllead for only a few years, relatively). No group of men in the lead trades has been investigated so thoroughly as this. The following facts have been established beyond the slightest doubt. The response on the part of the urine to the absorption of tetraethyllead is prompt and clearly indicative of the rate and extent of such absorption. This is, in fact, the means by which hygienic control and freedom from lead intoxication have been maintained. (Some of the evidence has been published, but it has been too voluminous to present in brief articles. I have been gathering the data for a monograph on the entire situation.) The lead content of the blood, in association with the absorption of tetraethyllead, on the other hand, is valueless in determining the rate and extent of the absorption. Even in fatal tetraethyllead poisoning, the concentration of lead in the blood remains within normal limits, at a time when the urine may contain 1 to 3 μ g. of lead per liter.

I have avoided the discussion of these matters in the part of this report which I submitted originally, for such editorial change as might be desirable, not because there is not much useful information, but, rather, if I may repeat, because it is

KE 0004705

Dr. John Ludwig - (2) - July 22, 1964

irrelevant.

The third paragraph of Dr. Goldsmith's letter, in my opinion, makes no useful contribution to the discussion. It would, indeed, be advantageous to have more and better information than is now available on the "body burden" of lead under varying conditions, and to have some feasible means of obtaining such information from the intact (living) organism. This we are attempting to do, with true precision, but we have not achieved this objective as yet, and I see no advantage, at this point, or in this report, of discussing it in relation to the most difficult phase of the problem - namely, the minor variations that occur among persons in the "normal" group. We know full well the general facts in this matter. What we do not know are the numbers - the quantitative relationships in precise mathematical terms. We shall never obtain them by wishing for them. These general facts are these:

(1) The body burden increases with every increase in the current level of the absorption of lead. That is, there is an equilibrated relationship between the intake, the output and the retention of lead in the body. In the simplest terms, the body burden is low when the current rate of intake is low; it is relatively high when the current rate of intake is relatively high.

(2) The best clue which we have to the quantitative relationship in the intact human body is the concentration of lead in one of the tissues (which are in equilibrium with each other) namely, the blood. The mathematical expression of this relationship, considering the variable rate of the metabolism of lead in the several tissues, especially in the skeleton, cannot be stated at present. I believe it will be possible, soon, to put this relationship into a mathematical form which will give reasonably adequate expression to the principal relationship, i.e., that which exists between the blood and the skeleton (this is the important one quantitatively, for the reason that under any set of circumstances involving inorganic lead, from about 90 to about 95 per cent of the lead in the body is found in the skeleton). If, therefore, we can find an indirect means of getting at the lead content of the skeleton, we shall know, for all practical purposes, the "body burden" of lead.

Now, I submit that no useful purpose will be served by including this discussion in this report, and for this reason I left it out of my assignment.

I regret that I must also object to the next paragraph of the letter. What John says here is definitely untrue. It is only when the exposure to lead is intermittent and at the same time abnormal (as in occupational exposure to lead) that a new level of equilibrated "steady state" is reached. If the exposure is significantly above the usual or normal environmental level and is maintained constant, accumulation of lead in the body occurs at a constant rate which is determined by the extent of the departure from the usual (normal) level. It is possible that a new level of the "body burden" is reached ultimately, but there is no evidence, as yet, that this occurs. The presumption is that the body burden continues to increase. This is, precisely the problem of lead in food and drink and in the ambient air. These represent continuous (albeit somewhat variable) exposure, and, as such, they have to be appraised against a lifetime (the human lifetime) with respect to their potentialities for harm.

John's comments with respect to the section on Lead Intoxication seem to me to

Dr. John Ludwig - (3) - July 22, 1964

confuse the issue of what is lead intoxication. We are not talking about exposure or the criteria of exposure or absorption, but about clinical plumbism. What has been said on this subject is just about as simple and factual as it can be made. Obviously, there is much more to be said, but a monograph would be required to say it. In my book, the excretion of porphyrins significantly in excess of the normal range, when it results from the intervention of lead in the maturation of hemoglobin, is lead intoxication. I have never seen any evidence of an increase in the excretion of porphyrins in relation to the absorption of lead, until a critical degree (range) of absorption is reached. I cannot be that certain about the juvenile forms of erythrocytes, since they represent a non-specific response to a variety of stimuli (to a much greater degree than that of the porphyrin metabolism), but the fact remains that they are, in fact, important phenomena in the clinical manifestations of lead intoxication.

I offer no objection to the alteration of Table VI-C-1 and VI-C-2 as proposed by Dr. Goldsmith. I do not agree that the last two columns in these tables tend to confuse the facts, but they do not contribute anything that is not evident otherwise, and that is enough for me.

If I may summarize, in one brief statement, all that I have said above in detail, I recognize that the discussion in C. Effects of Lead on Man is brief, and that there are many points that have been omitted, and many more that could be discussed at length. It was my purpose to state the facts in the briefest, simplest and least arguable manner. This, I thought, was necessary, and I have not changed my view. If the comments of Dr. Goldsmith are injected into this discussion, a great deal more will have to be said, as I believe my letter will indicate. I would consider the enlargement of this report, to this extent, to be wholly unjustified.

Sincerely yours,

RAK:vr

Robert A. Kehoe, M.D.

cc - John R. Goldsmith, M.D.
John Hage
Robert Horton, M.D.

Handwritten note to Dr. Goldsmith -

John: I'm sorry to have to differ with you so nearly completely, but I do consider it necessary to do so. I was very careful in my write up of the matters you criticize not to say anything that was not fully documented. There is no point, so far as I can see, in talking about the desirability of knowing more about the body burden, or the method of securing this information. The latter is not so simple as you suppose. You can indeed analyse bodies, but how can you determine the factors which have influenced the quantities found? Because of this difficulty which is virtually insurmountable, we have resorted to dynamic balance experiments to obtain the answer.

RAK