

ANNALS of Internal Medicine

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Edward J. Huth, M.D., *Editor*
Edward C. Rosenow, Jr., M.D.,
Executive Vice President
Fred C. Dauterich, Jr., *Business Manager*

4200 PINE STREET, PHILADELPHIA, PENNSYLVANIA 19104 USA
215/ B ARing 2-8120

Re: Ms. No. 71-617 by Browder, Louria and Joselow

The following comments and opinions apply, in the opinion of this reviewer, taking the points in the sequence of their occurrence in the review article:

1. The reference to mass screening (page 1) as a means of identifying "lead poisoned individuals, without overt disease," is a veiled statement about "subclinical" lead poisoning. It is a clue to a false point of view about the disease. How does one diagnose "subclinical" intoxication? Answer: by inference based upon obscure evidence of "impending" or "potential" disease, based upon apprehension. Unknown threats are still - in modern man - the most formidable to contemplate.

2. "Toxic manifestations of high blood levels" - page 1, paragraph 1. There are no such manifestations. There is no level of lead concentration in the blood or any other tissue or body fluid which denotes toxicity. There is danger of illness above a certain concentration, above which all cases of illness are found, but one sees levels three or four times the threshold level (at which the occasional case occurs), without any indication of illness.

3. "Everyone is exposed to lead as a by-product of industrialization" - first sentence under "The Sources of Lead." The fact is that lead was absorbed in some quantity (no one has any real idea of how much) by the first men who walked on the earth. Lead is in all soil, all water, all plants and all animals. How much as compared to now? Only speculation, such as indicated in reference 4, can begin to approach this matter. One must not be so gullible about this marvelously complex earth of ours. Industrialization has certainly added to the environmental availability of lead but the quantity which reaches man is still quite small. How does one differentiate between the effects of the absorption of a little lead from a still smaller quantity? This is what we have been trying to do, with a fair degree of success, but not yet enough. The issue is much too subtle for these authors fully to appreciate. The approach is in the realm of philosophy at first, and subsequently a matter of experimental technique involving the study of the universe.

4. "It enters the body with the intake of air, food and water." This statement requires critical analysis. There is very little evidence of the contamination of the ordinary food supplies of man with lead from ordinary environmental sources. The ^{edible} vegetative products used by man, in contradistinction from the forage of animals, is mainly in the form of the fruits and roots, which suffer little change in their lead content from surface contamination of plants. The lead in animal products used for human food is mainly in the skeleton while the muscle is very low in its lead content. The food chain of man is obviously invaded by processing, ~~grinding~~, but it is remarkably free of environmental contamination above that derived from the soil. This is a blank acceptance of an idea which takes little account of the sources and handling of human food.

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5. The statements about leaded gasoline are not entirely true (paragraph 1, page 2), but are more or less inconsequential. They demonstrate only a degree of inaccuracy in flat statements which is an indication of a degree of carelessness or of inadequate insistence upon complete information. The information has been published.

6. "The average adult in a city absorbs about 50 per cent. of the 30 to 40 μ g. of lead which he inhales daily." Actually, some 35 to 50 per cent. of that inhaled is exhaled under the conditions of ordinary respiratory activity. It may be as little as 30 per cent. or as much as 70 per cent., and the amount inhaled varies considerably with one's location and performance (home, indoors, asleep, etc.). No one knows the average inhaled. As to absorption, it is simply assumed that one absorbs all that is retained. This is probably untrue, but the amount cleared from the lung into the alimentary tract where absorption is poor is unknown. One does not make such statements on actual data.

7. "That 'the lead is almost fully excreted in bile and urine' has not been demonstrated and that this modest intake may increase blood levels substantially" is almost certainly entirely untrue. It has not been shown that the inhalation of lead in the ambient air (as differentiated from that in industrial establishments) elevates the concentration in the blood measurably.

Enough has been pointed out above to indicate that the authors have not studied the problem enough to appreciate the gaps in our knowledge. The manuscript abounds in such not necessarily untrue, but almost purely inferential conclusions based on half knowledge. The literature covered has been dealt with often in this matter, and despite its enormous volume, and its pseudo-scholarly nature, it has not been fully digested.

Not to be or even to appear carpingly critical of minor details, one passes on to more definitive issues. For example, much is made of the wide variations in the susceptibility of man under different conditions and at different ages. This has been the convenient explanation of necessarily incomplete information about lead vs. people for generations. It still remains so in certain medical circles, whereas the availability of means for the quantitative measurement of absorption (poor as they are sometimes after the fact) has served to demonstrate a remarkable similarity of human behavior when the facts are available. This is not to say that variability does not exist, but to insist that it is limited, except under extraordinary circumstances - essentially organic variability. There is simply no comparison between the exposure to lead in the ambient environment and that in even well controlled industry - in the quantitative sense.

But to skip over many pages and to deal with the "Definition and Determination of Lead Poisoning", here one runs the risk of losing his way entirely. Lead poisoning is defined as a clinical entity or series of entities; it is also defined in terms of a level of lead concentration in the blood, in apparent failure to recognize the stern fact that various laboratory tests - lead in urine, lead in blood, response to

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chelation therapy, deviation in the quantities of metabolites in the urine - are merely measurements which indicate the degree of the absorption of lead directly (when lead is measured), or indirectly when some precursor of a porphyrin or hemoglobin is measured. It does not follow that the impairment of a specific enzyme system means illnesses of the body, for there are often reserves of mechanisms in the body which counter adequately the impairment of another mechanism. We are just beginning to understand some of the "goings on" in the internal media of the body, in relation to lead, and although this is pointed toward an understanding of these mechanisms, it is no time for pronouncing on their immediate relation to illness. The difference between illness and the likelihood that illness will occur are two different things. Surely the physician, in recognition of some of our ignorance in these matters knows the difference in a pragmatic sense, however much he may have to ponder over the significance of biochemical phenomena, as bases for preventive measures. In the presence of actual illness, the necessity for a conclusion based partially on inference is obvious, but the business of finding illness when none is apparent, smacks a bit too much of clairvoyance to be trusted.

Finally, let me say that the temptation to expand our present knowledge of this subject into the realms of the unknown is admittedly great when we as physicians are confronted with the responsibility of interpreting an environment which only recently (in comparative terms) has been found to be potentially unfriendly (because we have made it so, in part). I do not assume an hypercritical attitude toward any of our colleagues, for indulging in this understandable exercise in the face of an entire population of mankind which is threatened, or for acting on their impulses. Within our own midst, however, as persons responsible for the health, and much of the well-being of this nation, we must be fairly sure of our position, and be capable of separating what we know, from what we hope to know in the near or far future. It is in this attitude of mind that I wrote in this instance.

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The Editors

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July 30, 1971

Robert A. Kehoe, M.D.
Kettering Laboratory
Eden and Bethesda Aves.
Cincinnati, Ohio 45219

Dear Dr. Kehoe:

Re. Ms. No. 71-617

We should like very much to have you or one of your colleagues give us a critical opinion of this manuscript as a paper for possible publication in the ANNALS. If you will not be able to review it and return it to us within two weeks, please feel free to return it immediately without a review, using the enclosed envelope.

If you can give us comments on this paper, please have them typed on the enclosed blank sheets, and return two copies, together with the manuscript, to us. Do not sign your name or indicate who the reviewer is on the "Reviewer's Comments" sheets; this permits us to send one copy to the author without transcription.

Thank you very much for your help.

Sincerely,

*P.S. This paper is submitted
for consideration as a review
article - it should be
judged accordingly.
EJH:jp
Enclosures*

Edward J. Huth
Edward J. Huth, M.D.
Editor

Title: LEAD POISONING, NEW INTEREST IN AN OLD PROBLEM

By: Drs. Browder, Louria, and Joselow

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