

May 9, 1969

P.S.I. Barry, M.D.
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Ellesmere Port, Cheshire
England

Dear Pat:

I am returning your manuscript herewith, along with two tables and two charts for such use as they may be to you and Dr. Mossman. I am commenting below on various things in the manuscript and in the tables and charts.

First, let me say that the tables and charts are not necessarily suitable for your paper, since there are other ways of presenting the same things, as you have shown in your tables and charts. I chose to set up the data according to my own way of examining them and they reveal certain things to me of which I had not been fully aware before. I'll point these things out below.

I have also made certain notations and suggestions which, for the most part, represent my way of expressing myself. I realize that these are not strictly in accord with British practice. Make use of any of them that seem useful and discard the others. I shall deal with these first.

(1) The editorial changes or corrections (if they may be called such) are self-explanatory, I believe. My long practice at this has a compulsive character.

(2) On page six are a series of more (to me) important matters. The first has to do with the use of the word "steady" which implies that you can visualize the increases as developing at a regular rate over a considerable period of time. This, I think, is an error in the employment of a term, rather than one of judgment, but it gives the wrong impression. It is entirely possible, and I think it more likely, to visualize these as being the result of quite irregular short or long periods of exposure to lead at an unusual rate, the results of which are found only in the skeleton and, specifically, to a much greater extent, in the long (dense) bone. I charted the individual results according to the age of the subjects on the two attached scatter graphs, because I wanted to see how they disposed themselves. It can be seen that the results within any age group are distributed all over the area, fanning out the more widely as time goes on. This, I think suggests that the experience (exposure) of these individuals varied widely in time and severity. A generalization can be stated to the effect that the longer one lives the more likely he is to encounter periods of unusual exposure to an element which is ubiquitous in one's environment. Thus, the males yield a record of greater (more frequent and more severe) exposure, because of the very nature of their daily life. My point is this - this can be interpreted as occupational exposure in some instances and as environmental exposure in others. But it can hardly, by any stretch of imagination, be an expression of the lead content of the ambient atmosphere; rather it is the total expression of episodic contacts with lead in food and beverages, and in air-borne lead inhaled when doing various jobs at home or at one's customary work-place.

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(It is nothing short of amazing to me that the general results are as low as they have turned out to be. Look at the distribution of the frequencies of the occurrence of various concentrations in the bones of both males and females; sixteen of the 26 females have yielded quite low values in the flat bones, while all but three of them have provided results in the long bones within the range of our (very small) normal group. Moreover, the latter group is strung out over a surprising long range of frequencies, which also is indicative of highly variable experience in both time and severity.)

(3) My next query of statements on page 6 relates to the "levelling off." If you examine the scatter charts, you will find little evidence of a levelling off. I conclude, therefore, that the determination of an average value for the results obtained within a specific decade is an artifact. One or two high values can run it up, while one or two very low values can run it down. The actual result in each instance is a matter of chance, so that a large number of results would be required to represent human experience up to a certain age. The scatter chart, therefore, is a more realistic expression of the true or weighted value of each result. It also takes account of the fact that the record of past experiences is "locked up" in the long bones as time goes on. (This same objection applies to the presentation of Tipton's data in the article of Schroeder and Tipton.)

(4) My next item on page 6 concerns my inability to understand what is being said in the last sentence of the third paragraph. If you should consider, as I do, the effect of a fairly common level of exposure to lead in what may be called the general environment (recognizing the greater quantity and variety of the food and beverages consumed by the male member of the family), to which is added the greater number and variety of the opportunities for exposure to lead by many of the males, away from home and en route to and from work, you will conclude, as I do, that the average of a few individual results within an age-group, is a very fictitious result. It is not a greater general level of exposure, but a wider range of experiences giving rise to varied types of exposure at varied intervals and for periods of varied duration, each of which is "recorded" to some extent in the lead content of the bones, with special emphasis upon the long (dense) bones. There is one outstandingly high result in the long bones (221 parts per million, or as I generally express 22.1 mg. per 100 grams) as analysed in their fresh state. You will note that this man discontinued his obviously severe exposure at least 17 years (and perhaps 24 years) before he died, and yet had a very high body burden of lead largely "fixed" in the dense portion of his skeleton.

On page 7, at the bottom of the page, is a very important bit of information, as indicated in the margin. I have commented on this previously, and so need not do so again, except to point out the "protective" influence of the hard or dense part of the skeleton in removing the bulk of the body burden (that resulting from past severe exposure) from active engagement in the continuous metabolic processes (shifts to other tissues and into the excreta) of the body.

The marked paragraph is questioned on page 8, not because of doubt but because this, so far as I know, is a matter which has not been noted before (I may be wrong and perhaps you should check this). It is evident that in the very youthful skeleton, corresponding to what we know about the maturation of the skeleton, there is very little dense bone, so that the soft tissues are not so well "protected." This may be a very important matter in relation to the response to the severity of exposure.

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It is a factor which I have not taken into account previously, and it is worth mentioning in your discussion. In addition to this point, it is important to have found no differentiation in the sexes. This would seem to be explained adequately by the similarity of the dietary and other environmental conditions of the two sexes in their early life.

Your comment in the fourth paragraph on page 8 is well taken with respect to the comparison of your findings, as to body burden, with those of Schroeder and Tipton.

I believe you said something about omitting any information about the hair and nails. I think, in view of the ideas of others as to the importance of this matter, that you might well report your data and leave extensive discussion of the matter until later. Under similar circumstances, I would be inclined to make some comment on the medico-legal aspects of this if the relationships can be explored sufficiently to relate the findings to the time of occurrence and the severity of the exposure. However, I would tend to discourage the efforts being made (by Japanese investigators, for example) to make use of analyses of the hair (especially) and the nails for the purposes of appraising the severity of occupational exposure to lead. Perhaps, however, you will prefer to postpone such comments.

In your conclusions, reference is made to the accumulation of lead in the bone, especially long bone, with age - speaking of it as slower. As I indicated previously, this I believe is the wrong way to express this. You are not privileged here on the evidence available, to speak of rate but only of amount. You don't know that this accumulated slowly over a considerable period of time. You know only that it is there. It may have arrived there many years before at the time of a relatively severe exposure, and this is all that remains of what may have been a much larger quantity at some time in the past.

Finally, let me say that this is a good paper. The data are trustworthy, I believe. (I asked Jack Cholak to look at the analytical section just for the record), and a number of very interesting facts have been established. I'll be pleased to see the revised manuscript when ever you wish me to do so, but if you wish to go ahead and publish it without my seeing it again, do not hesitate to do so. You need not have any hesitation in presenting the data, while such discussion as you choose to provide will, I'm sure, be fully justified.

With kindest regards,

Sincerely yours,

Robert A. Kehoe, M.D.
Professor Emeritus of
Occupational Medicine

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P.S. We were delighted to receive the card from Anne from Cornwall.

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