

June 22, 1970

P.S.I. Barry, M.D.
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Dear Pat:

I am glad to be able to comment on the paper of Dr. Jennifer A. Thompson which is concerned with "THE BALANCE BETWEEN THE INTAKE AND OUTPUT OF LEAD IN NORMAL INDIVIDUALS." I shall do so carefully and fairly critically, for the reason that, while this is a good piece of work, for which Dr. Thompson deserves commendation, it goes somewhat beyond the appropriate conclusions, for which, while she is well within the company of many others, she should be well advised to back up a bit.

I shall not advise Dr. Thompson on how to express herself, but rather point out, in general terms, wherein she has misstated or overstated her case in some measure. In doing this, I am accepting the data as they have been arrived at by the methods of sampling and analysis. I realize, of course, that there are many difficulties associated with this type of experimentation, and that the opportunities for error by subjects of unimpeachable intent are numerous, especially in the duplication of each day's intake of food. I must assume, as must everyone of good will, in matters of precision, who explores this situation, either by carrying out the work or by the examination of the data of others, that the facts as obtained are essentially true, plus or minus some error, hopefully of modest proportions. Not all subjects of such experiments are technically intelligent, or sufficiently devoted to accepted duty, to avoid slight errors. Consequently, the results obtained cannot be trusted to convey the whole truth and nothing but the truth. Furthermore, even if the experiments are conducted by the subjects with meticulous care, the failure to obtain and measure certain quantities of lead taken into the body, and certain others which are put out of the body, leave something to be desired in strict "balance" experiments. Not only is lead taken into the body via the respiratory tract, from which some escapes in the expired air, and from which some escapes into the alimentary tract via the movements outward from lungs and passages (that is, in ways which at present we are unable to measure precisely), but also some enters the mouth - other than in food and beverages - from chemically unclean objects (fingers, etc.) put into the mouth. Considering the fact that lead is all around us, and as dust on everything which we touch, it is very difficult to avoid some contamination (probably slight as a rule, but not always). As to output, the same type of lack obtains, in that everything that leaves the body is concerned - mostly of course in the feces and urine, also in sweat and other cutaneous secretions, in desquamated skin, broken and clipped nails and falling and cut hair, as well as all other discharges from the body. Since the entering lead from all sources excepting that of the food and beverages, under ordinary circumstances, is small, and since everything that is discharged from the body, other than feces, is usually correspondingly small, we are prone to disregard the smaller items on either side of the equation. Nevertheless, we must regard both intake and output as plus or minus the values obtained by analysis, and especially in the lead

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content of the duplicate food sample, in some doubt. Therefore, when the variability of these values, day by day, is high, we must look at the small differences with a fishy eye, level out the variability, as well as the errors by statistical means, and then turn to other evidence - lead content of entire bodies of different age groups, for example - before being too sure about the precise degree of the balance or the retention.

It will be remembered that in the two balance experiments which we carried out with particular care, there was a slight and uniform difference between intake and output over the period of 13 months in one instance and 18 months in another. This difference favored the output to the extent of about 8 milligrams of lead per year. Admittedly, this may have been due to the combination of errors of which I spoke above, including, perhaps, (but unlikely) some slight systematic analytical error, but the trend throughout the experiment was too uniform to be a matter of chance. The quantity was simply too small, within the universe of human performance, to be fully trusted. But the two subjects of these experiments were competent and well informed technical men who did their best to avoid mistakes. Moreover, our tests of the analytical procedures has yielded no evidence of systematic error, but rather of both positive and negative error, which should cancel. So I am constrained somewhat to regard the results as valid, unless and until they can be made to appear unlikely or invalid.

With these ideas in mind, I cannot accept as fact the retention of lead by four of five of these subjects. The fact that one put out more lead than he took in, under the experimental terms, and that the others varied (as indeed, they must have) in the quantities of the difference between intake and output, brings the results into greater harmony with our own. That is, the facts obtained in this manner by the investigation of five persons only, for short periods of time fit nicely into the universe of our own more numerous and more prolonged observations. (There is, indeed, a seasonal variation, perhaps confined to the temperate latitude and to the topography which characterize Cincinnati.)

As may be gathered from our experiments and my writings, I have reasons to doubt gravely that so-called normal persons in the so-called normal ambient environment accumulate lead in their tissues in any such quantities as is inferred in the report of these experiments. The truth or falsity of this matter is an extremely important one, so that one may not arrive at conclusions in such a matter by inferences. These observations, therefore, are very much more important than they have been made to seem in this report, but, paradoxically, they do not lend themselves certainly to the conclusion that the imbalance portrayed here actually existed. Nor do they prove that the retention of lead was of the order of magnitude which it might be thought to portray. These matters, I think, should be made clearer than they are in the paper supplied to me. To clarify them will not in any way render the results less important, but will demonstrate a degree of balanced judgment in the investigation, which will redound greatly to her credit.

I have made certain comments, and have suggested certain alterations of the text. So as not to alter the author's final text (which I would not presume to do), but rather to indicate, in a general way, what I would say. I have noted these with a pencil, which permits erasure without more than a trace of smudge. With this

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addition to my general criticism, I have given the author my views in an entirely frank manner. This should not convey the idea to her that I disapprove the work. To the contrary, I consider that this was an excellent piece of work, for which, as part of her credentials, I would be pleased to award the doctoral degree.

I shall write to you on other matters as soon as I can find time to do as I like. At present, I am grinding out the editorial work on the papers of the Amsterdam Conference.

Best regards.

Sincerely,

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

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