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September 11, 1968

Mr. Carl Thompson, Senior Vice President
Hall and Knowlton, Inc.
150 East Forty-Second Street
New York, New York 10017

Dear Mr. Thompson:

Pursuant to the promise in my letter of July 5th, in responding to yours of the first, I am citing some references to pertinent literature, and am sending you certain reprints.

I send also a copy of the monograph of Aub, Fairhall, Minot and Reznikoff, which, published in 1926, was the gospel according to Harvard and, in the minds of many, few of whom have read it at any time or recently, continues to be regarded as a monumental piece of work. Let me say that it represents a very stimulating bit of interpretation, despite the incorrectness of the principal thesis concerning the "mobilization of lead," so that there is some justification for its acceptance aside from its origin in the Harvard Medical School. I think you should examine this as completely as may be necessary to learn the state of the analytical methodology of the time, and to perceive the comparison of the knowledge of the time with that now available. This may be a chore for you, and if I am posing an unreasonably difficult task, you will, I am sure, appreciate my purpose. I think it would be difficult to obtain a copy of this book at present. It belongs to the library of the Laboratory and should be returned.

I am also sending you a volume which I put together many years ago for consultants of Ethyl Corporation, comprised of a series of published articles from the Kettering Laboratory, together with the "Regulations" relating to mixing operations. Reprints of the publications are now out of print. Moreover, the copies of this that were distributed, have disappeared into limbo for the most part. I had four volumes a little while ago (several years), but this is my last copy. Please be careful of it and return it as soon as it has served your purpose. I call attention to certain parts of it that will probably be of interest to you in connection with various aspects of the matter about which you inquired, as follows:

Page 289. Note the protest of Fairhall as to criticism of his analytical methods, despite the fact that the time these data were published, the methods had been found wanting by several investigators. He did not admit his error until many years later, and then only partially. I mention this only because this high-handed tenacity was a factor in the persistence of the thesis about "mobilization." The comments in the preceding articles with respect to the analytical method were not unduly critical, so that Fairhall's reaction to them was indeed an over-reaction. This note of his was published because the Journal in which we published was edited at Harvard by Phil Drinker. Fairhall literally badgered him into the insertion of this note, within the articles, at the time of their publication - a procedure which was certainly very unusual. He even undertook to prevent their publication in J.I.H. to which Drinker would not agree. The real issue, of course, was the matter of finding lead in virtually everything and everybody, against the statements and the discussion in the monographs of Aub et al. See pages 55 and 56.

Page 320. This article gives the early graphic evidence of the continued excretion of lead in the urine of persons without unusual exposure to lead, and the greater excretion in the urine of persons who had been exposed but now under observation were eliminating that which had accumulated. It is obvious, considering the distribution of lead in the body (90 percent or more in the skeleton) that most of the excreted lead was being released from the skeleton of the previously and severely exposed persons. The meaning of this, of course, is that the skeletal lead is not "locked up" or so bound chemically as to be inert, but is participating actively in the metabolic process whereby it is being lost from the body, after the exposure which induced its absorption came to an end. This was the first concrete evidence submitted to demonstra that lead in the bone "mobilizes" itself - that is, is metabolized physiologically. The question thus arises - can this process be speeded up by chemical means? We attempted to do this by the methods proposed by Aub et al. (see Chapter IX, page 98 of monograph). Especially the summary. Note that the experimental evidence in support of the hypothesis of "deleading" was obtained not from analysis of the urine (for which the analytical methods were insufficiently sensitive), but by analysis of the feces in which the lead found is due to the ingestion of lead in food and beverages The liver, fed as a part of the low-calcium diet, is higher in lead than any other tissue in the animal organism with the exception of the skeleton.

Now for the examination of the therapy for mobilizing lead, as advocated by Aub et al. The trials applied to patients have not been published, and I see no reason for publishing them, in view of the information available from observations made experimentally on human subjects. In the latter connection, I am sending you two other publications. The one is the smaller of two blue paper-back publications, entitled "Lead Poisoning Symposium," in the last article of which there are recorded, briefly, the results of a series of observations on the intake and output of lead on the part of an experimental subject in whose case a series of dietary changes were introduced in our effort to promote singificant changes in the loss of retained lead from the body. You will note the text beginning with the last (incomplete) paragraph on page 76, and extending on through page 77 down to the last (incomplete) paragraph.

On page 78, first complete paragraph, beginning with the words "During the fifty-seventh month," is a brief description of an attempt to promote the "mobilization" of the approximately 110 milligrams of lead that had been retained during the entire period of the oral administration of lead, by the use of the method advised by Aub, namely - the administration of ammonium chloride (to produce a shift in the acid-base equilibrium of the subject) in large dosage over the period of two weeks during which both calcium and phosphorous were held at a low level in the diet. You will note that a slight increase in the urinary output of lead occurred at this time - that is, within this 30 day period, without increase in the concentration of lead in the urine. This occurred during September running into October, when the cooler weather in Cincinnati yielded an increase in the volume of the urine. The response to the "therapy" was utterly negligible.

Note also the marked passages on page 79, which, at that time, were made conservatively. Later, more significant observations were made on "leaded" industrial employees with similarly negligible results. (This is very nearly the last copy available, of this reprint. Please return it).

The other "blue book," is a copy of the Harben Lectures in which further reference is made to these same experiments. See top of page 37 et seq. Other evidence of the stabile character of the lead metabolism is presented and discussed. I commend this publication (which you may keep) to you in evidence of the predictable pattern of the

* Or to lead administered by mouth, or to that trapped in the upper respiratory tract, collected in the naso-pharynx and swallowed.

handling of lead in the human body.

There is an additional unpublished experience relating to groups of workmen in the tetraethyllead plants in Baton Rouge and in Deepwater, New Jersey. In one of the years during which we had a severe epidemic of influenza (I have not bothered to look up the year in my records), we had a degree of concern lest this acute, highly toxic illness should be accentuated by the men who were running relatively high in their urinary lead. Many of the men were ill and unable to work. Their urinary excretion of lead was watched, and good contact was maintained by the respective medical personnel with the employees. There were no fatalities, no complications, no really dangerous cases of illness and do evidence whatever of significant changes in the urinary excretion of lead. (This, of course, is not the same situation as that of men exposed only to the inorganic compounds of lead. However, among those employees were men who worked in the production of alloy where they were exposed to metallic lead and inorganic compounds of lead, and in the furnace area, where much, if not the greater part, of the exposure to lead is of inorganic type.) I have had no hesitation since this experience, in advising all who consulted me, that they need have no special fear of infectious disease processes as factors in the mobilization of lead. I have never had to retract or apolize for this advice.

The references to the public acknowledgment, by Fairhall and Aub, of their inability to reproduce in animals or in patients or other human beings, the "mobilization" of lead, as referred to in their experiments, will be found in the following comments. You can obtain these articles readily in the libraries available to you in New York.

Aub and some of his associates published two articles in the A.M.A. Archives of Industrial Hygiene and Occupational Medicine, Volume 9, 1954. The first of these can be found in pages 9-22, while the second is on pages 113-121. The respective titles are "Comparative Exchange of Calcium Lead and Radioactive Lead in Dogs" and "Migration of Inorganic Salts in Bone as Measured by Radioactive Lead and by Alizarin." This work was done in 1937, but the publication of the articles was delayed until 1954, partly, at least, because Aub found it difficult to explain why the lack of effects of the "deleading" procedure in these experiments was so different from that of the earlier experiments. The reason (which he never admitted in print) was that he and his group were using methods for following the radioactive lead that yielded accurate and readily interpreted results, while his prior work was based on the poor analytical methods then employed and also upon a physiological misconception of the avenues for the excretion of lead from the body. This misconception had existed for many many years and in many minds, so that it is excusable until suitable physiological and analytical methods had been applied to the problem. The error is now readily visible and explainable, but unfortunately, few would-be investigators go back to find and understand the errors of past experimentation and interpretation.

You will find the first of these articles to be worth examining in connection with your question of documentation. Note the data, the "Comment" on page 18, and the "Conclusio especially the second and third paragraphs. The lame attempt at the explanation, seventeen years after the finding of the discrepancy, by which time our balance experiments had demonstrated the facts, is an important feature of the doubts that exist in the minds of many people who have not followed the experimental work in any detail.

The second article may not appear to be of much interest to you, but it is important in demonstrating that the radioactive lead (aside from the effects of radiation on the

animals) behaved in the body of the animals just like the inert lead. There is not a leg to stand on, therefore, in attributing unusual metabolic behavior to it, in relation to a response to the administration of the parathyroid hormone as a deleading agent. Here is where the work of Aub and Hunter, done years earlier and still referred to by persons who are not familiar with the sequence of events, went down the drain.

An article by Lawrence Fairhall (then in the U.S. Public Health Service, formerly the analyst for the Harvard group) and Paul Neal (a good friend of mine who reported these results to me prior to their publication and also his difficulties with Fairhall) appeared in Public Health Reports Vol. 53, Part 2, pages 1231, 1245, 1954. Fairhall had found it very difficult to adapt himself to the use of the dithizone method of analysis (since his own was faultless), and neither of these men had tumbled, at this time, to the fact that the true excretion of lead in the feces (as compared with that which represented lead in transit in the alimentary tract as the result of the ingestion of lead with food and drink and that administered) was not as great, at times, as that in the urine. Therefore, the importance of the response, if any, of the rate of the urinary excretion of lead, to "deleading" therapy, was not emphasized as it should have been. A look at the third section (from the top) of the graph on page 1238 will show, however, that nothing of consequence happened when ammonium chloride (B) was administered during a period of low calcium intake. Note the second paragraph of the text on page 1232. (The idea died hard.)

You may think that I am being a bit hard on the Harvard investigators, especially on Fairhall, in my comments, aside from those of scientific purport. It may be that this is the case, and, if so, perhaps I can be forgiven for some feeling in this matter in connection with my efforts to reveal the truth in those matters during the past forty years. The more important aspect of the matter is not any wish on my part to promote personal bitterness or past controversies, but is rather the necessity of pointing out the errors in methodology and interpretation which have resulted in certain of the present conflicts of opinion. Any one who does this is being unpleasant and combative, by current criteria of behavior. So let it be.

Sincerely yours,

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

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