

July 5, 1968

Mr. Carl Thompson
Senior Vice President
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150 East Forty-Second Street
New York, N. Y. 10017

Dear Mr. Thompson:

Your letter of July 1st raises an issue to which I shall respond shortly, in the manner of your request, by supplying you with references, and so far as possible, reprints. This will take a little time of which I am in short supply, at the moment, but I'll get to it soon. The trouble is that the documentation of my statement, which has been well known to some of my colleagues, occurred in bits and pieces some fifteen to twenty years ago and now has to be sought out piece by piece. You will be interested, however, in knowing that both Joe Aub and Lawrence Fairhall (Harvard), who were the instigators of the idea of the mobilization of lead from the skeleton through metabolic disturbances, published later and meager accounts of their failure to verify their original hypothesis.

I think you should know the physiological background of the concept, and of the demonstration, later, that the concept, almost in its entirety, was fallacious. I think you should know also, how the false concept came about. These are matters which very few of the would-be experts on this subject have bothered themselves to review and learn about.

In the early twenties, Joseph Aub, M.D., and his associates at Harvard carried out a series of experimental investigations under a grant of funds from Lead Industries Association. This was before the development of analytical methods of sufficient sensitivity to deal with a few micrograms of lead in any specimen. Consequently, they could not, and did not obtain data on the urine or blood of experimental animals and men. (It was not until the middle thirties that a suitable method for the determination of lead in the blood came to be available.) They were able to determine the presence of lead in the tissues and the feces of animals to which lead had been administered (with reasonable accuracy in the skeletal tissues, since most of the lead was to be found there), but they concluded, mistakenly, and so stated, that lead did not occur in human tissues and excreta unless there had been some unusual type and degree of exposure, as, for example, occupational exposure. They concluded further, only partially correctly, that lead absorbed in detectable quantities found its way into the skeleton, where it remained locked up, so to speak, until and unless some disturbance in the metabolic process in the body "mobilized" it. Such mobilization could be induced in experimental animals (cats mainly were used in their experiments) by a variety of procedures, e.g., the administration of ammonium chloride (to induce a shift in the acid-base balance in the body to the acid side), the restriction of calcium (which tended to call upon the store of calcium in the skeleton and with this the release of lead in the skeleton as well). Other disturbances that would cause major shifts in the acid-base equilibrium of the body could be counted on to have the same effect as the administration of acid. (I should explain that the ammonium in ammonium chloride is readily metabolized in the body, leaving the chloride to attach itself to fixed bases (Na⁺, K⁺, etc.) with which it is excreted, thus diminishing the basic elements

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in the body.) By inference, and without adequate supporting evidence, physiologic and disease processes that tend to promote an acidic condition in the body, as fatigue, infectious disease, alcoholism, deep anaesthesia, and such stresses as pregnancy, were believed to induce mobilization, and hence to create the threat of the toxic effects of lead.

The evidence on which this hypothesis was based was that of determining the lead content of the feces of animals to which one or another of the "therapeutic agents" was administered. (It had been believed, up to that time, and actually until our observations had demonstrated the facts in the matter, that lead was excreted solely in the feces, and that there was no necessity for determining the lead content of the urine. Since also there was no grasp of the fact that everything eaten by animals and man contained lead, there was no thought of this as a source of lead in the feces. You can see how easy it is to follow the prevalent view. This tendency was so strong that in the initial field survey of the Public Health Service in 1924-25, no specimens of urine were collected, despite the evidence which Graham Edgar and I had presented in the May Conference. No one believed that these results were valid, because of the prevalent view, and because the Dean of Harvard Medical School ridiculed them /and never had the grace to admit his error/. Thus, the conclusions of the often commended investigation of the USPHS, in 1924-25, which "gave Ethyl a clean bill of health," were based on wholly irrelevant information, except to the extent that their physical examinations confirmed our findings that none of the exposed persons was ill. For obvious reasons, I never pointed out this fact in the literature. I was quite content to accept the "clean bill of health," since I had my own, and much better, reasons for believing it. The fact is that almost no one read the USPHS report, beyond the conclusions and recommendations.)

But to continue from where the parenthesis begins, let me point out that the experimental animals (cats) put on a low calcium diet were fed on liver as their principal dietary component, and that this item was sufficient to yield an appreciable increase in the lead content of the feces. It happens that the liver is relatively high in lead (not so high as the skeleton, but high as compared to other edible tissues). Hence the lead content of the feces of the animals on the experimental regimen (low calcium), as compared to control animals, was appreciably elevated regardless of the other therapeutic agents employed.

There is more to the matter than I have stated above, but this will be enough, I believe, to let you in on the facts. If you are keenly interested, you should read the reports of the investigators. Because this information, published eventually in a monograph, came from Harvard, it made a tremendous impression. Lead poisoning had undergone a monumental clarification. This was indeed, a major effort which deserved due consideration, and you will find that the work is still being commended by people who have no idea how thin the evidence. You may remember how Harriet Hardy defended the Harvard position at the Washington Symposium. There is not a shred of evidence that pregnancy, anaesthesia or infectious disease has ever precipitated a case of lead poisoning, and actually the burden should be on the believer of this hypothesis to adduce proof. Instead, because Harvard has stated the concept forty years ago, the burden has been on the dissenter to disprove the hypothesis. We have done so to the satisfaction of most industrial physicians, and that of all current investigators of the subject, but the idea persists among many clinicians.

As I have said, I'll dig up specific evidence for you in presentable form, but the principal basis for what I've said lies in the physiological facts which have been

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emerged from our balance experiments - those tedious, pedestrian observations which have demonstrated the nature of the behavior of lead in the human body over prolonged periods of time. As a physiologist, I found it necessary to do these troublesome and costly experiments in order to find out, once and for all, what happens under the variable conditions of day to day life. Their counterpart, in large groups of persons, young and old, healthy and partially impaired, has been obtained by over more than thirty years of investigation of very large numbers of persons in a wide variety of lead trades. I hope to be able to put this information together within the next few years. It has been too voluminous to handle while I was occupied in directing the activities of the Kettering Laboratory. Therefore, I have put out bits and pieces of "skimmed off cream" in several papers, principally in the Harben Lectures, which I felt compelled to assemble, when the opportunity was presented to do so, by the invitation of the Royal Institute of Health and Hygiene in London in 1960. If other matters would stand still long enough for me to get solidly at this job, it would be much easier for me to answer such questions as yours (and many others) in a documentary manner, rather than in ex cathedra statements. This is by no means a "nasty crack" at you, nor indeed at others who raise questions that require documentation. It is simply an expression of dissatisfaction at the state of many affairs in this troubled and troublesome time in which we live. There is hardly time to ponder, much less to set down in proper form the observations of most of a life time. People who know little, or at least too little for the purpose, continue to speak and to write and to make it necessary to do what reasonably and appropriately can be done to offset their shortcomings.

For example, I have just received a journal, SCIENCE AND CITIZEN, published by a Committee for Environmental Information, 5144 Delmar Blvd., St. Louis, Mo. 63108, said to be an official publication of SCIENTISTS INSTITUTE FOR PUBLIC INFORMATION (30 East 68th Street, New York 10021). The present number, Volume 10, No. 3, April 1968, is devoted entirely to lead, and is an excellent presentation of one side of the issue, with some slight attempt to present the other side. It came with a courteous letter from a Staff Writer, Joseph D. Salvia inviting me to comment on it. This, of course, I cannot do for publication. I refuse to be put on the defensive or to be involved in any other than a straightforward scientific discussion with scientists, unless there is an official (governmental) issue which must be met in a manner that is dictated by an agency or representative of government.

But enough of this. I am sure that you are aware of the problem. I am just a bit too sensitized by some aspects of it to sit quietly and patiently for time to work its way.

Sincerely yours,

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

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