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COLLEGE OF MEDICINE, EDEN AND BETHESDA AVENUES
KETTERING LABORATORY
DEPARTMENT OF ENVIRONMENTAL HEALTH

April 14, 1971

Louise H. Marshall, Ph.D.
Division of Medical Sciences
National Research Council
National Academy of Sciences
2101 Constitution Avenue
Washington, D.C. 20418

Dear Doctor Marshall:

When I last talked with you, I promised to send you information about some experimental work being done by a group in the Medical School of the University of Albany and I hasten to do so, since such information should certainly be known to your group. Obviously, what I have to say, while accurate, is not in publication at the present time, and should be dealt with by your group with that circumspection which applies to information obtained at second hand.

In order to illustrate what we and this group in Albany are attempting to do, I send you, herewith, an article which I prepared some years ago, for presenting at Vienna. You will note that the conditions of our experiment did not permit us to draw definitive conclusions. We, therefore, went to another experiment, at a higher level of exposure, in order to determine what would happen under these circumstances. We found this new level to be definitely too high to meet our criteria. Yet at the lower level, we were not able to distinguish what was happening because of the variability of the lead intake in food and beverages.

The above dilemna was solved when it was found that the group in Albany, by using a reasonably cooperative set of prison volunteers, and by making a large respiratory chamber of a hospital ward (in the prison) could maintain the experiment for approximately 22 hours per day (24 hours less the time required for eating outside the chamber, and for incidental purposes) on 7 days per week, could determine the actual facts in relation to virtually continuous exposure, over a period of 16 weeks. Fourteen men were so exposed at the level of 10 micrograms per cubic meter, while six were followed as controls, without any induced exposure.

In this work, animals, both monkeys and rats, were subjected to exposure to lead in a chamber well devised for the purpose, as a check on what might, perhaps, be expected to happen to people.

Both animals and men reacted to this exposure (10 micrograms was intended, but, actually, the concentration was just about 8.5 micrograms per cubic meter of air, being subject to a degree of variability from day to day, ranging from a little above 7 to somewhat above 9. This, in our experience, is just about as well as one can do, considering the analytical deviation, on one hand, and the manipulative variabilit in producing the lead sesquioxide, on the other.) In both instances (animals and men), the urinary output of lead tended to increase progressively, throughout 16 weeks of exposure. Likewise, there was a definite increase in the concentration

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of lead in the blood of both animals and men. In the case of the men, the blood level at the start was low (in keeping with the circumstances of the lives of these men as prisoners), ranging from 13 to 26 and averaging 19 micrograms per 100 milliliters. The values at day 107 (the final data are not now available) ranged from 28 to 42 and averaged 36 micrograms per 100 milliliters.

I have examined the methods, and I consider this work to have been done in a competent manner. In my view, this evidence means that the level of 10 micrograms in the air is too high to be regarded as permissible.

The experiment will be repeated (with new subjects) at 5 micrograms (as nearly as one can get and maintain the level), as promptly as possible, with due regard to analytical load and other factors.

Sincerely yours,

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

RAK:wb

April 8, 1971

Louise H. Marshall, Ph.D.
Division of Medical Sciences
National Research Council
National Academy of Sciences
2101 Constitution Avenue
Washington, D.C. 20418

Dear Doctor Marshall:

I write this letter to you to follow up the telephone conversation in which we engaged a few hours ago, and, to some extent, to put myself on record in your hands, with respect to certain bits of information, certain opinions derived from experience and experimentation, as well as certain personal and professional matters which have affected my performance in acting for your panel in relation to its report.

Before attending to the remarks made over the telephone, and to the notes made on certain sections of the Second Draft of the Report of the Panel, it seems necessary to refer to a matter which is of great importance in relation to the exposure of populations to lead in the ambient air, in that the latter, although variable in terms of both locale and respiratory behavior, it is a continuous type of exposure, which may be expected to exist over the period of a lifetime for the individual who remains in an environment in which lead is found in the air (this presumably is now everywhere) and in the food and beverages consumed. By virtue of the fact that swallowed lead remains within the human body for many hours with some change in concentration, the consumption of lead-containing food and beverages several times per day provides a source for the absorption of lead all day every day. On the other hand, discontinuous or intermittent exposure, such as that in industry, usually 8 hours per day, on 5 days per week, is less than 1/4 of the time, the remainder being free of exposure (or should be), so that an equilibrium is reached after 16 to 20 weeks (under the ordinary conditions of work and exposure when the conditions are maintained uniformly), and the concentration of lead in the urine and blood continue on a somewhat elevated plateau which is characteristic of the particular severity of the exposure. The latter is the primary medical basis (not the engineering) for the adequate control of the conditions in a modern well run lead industry, whereby no cases of lead poisoning occur, so long as the hygienic conditions are maintained. So recently (within the last 25 or 30 years) has the modern regimen been in fully controlled use, that most people, doctors included, have no knowledge of it. However, there are one-time hazardous industries, involving thousands of employees, in this country, in which there has not been a case of lead poisoning for nearly three decades. The same result is obtained in some industries and in which, under the present regime, none are expected.

Now, to go back to the continuous exposure, such as that involved in breathing the ambient air (or also in the ingestion of lead in amounts which exceed the ordinary normal condition, whether experimentally or by accident, such as the ingestion of food or water of excessively high in lead), any daily dose which is sufficient to increase the rate of the excretion of lead in the urine, or the concentration of lead in the blood will (so far as our experiments have shown in feeding lead for as long as 4 years at a specific rate), if maintained, result in a rate of absorption (which depends on

the dose) which is maintained steadily in a straight line relationship for as long as the dose is maintained. Here is where the criterion of safety, in the pollution of air with lead, must be based upon a concentration so low that it is incapable of bringing about a measureable increase in the rate of the absorption of lead, insofar as this is shown first by an increase of the excretion of lead in the urine, and later by an increase in the concentration of lead in the blood.

For some reason, which I simply cannot fathom, very few people, technical men or doctors, have found it possible to look at our experimental data and see this fact, which is as clear as the nose on one's face. I suppose the reason is that very few of them are physiologists who are willing to learn things that have not been known before. There is some mystery, it seems, about ordinary physiological phenomena, which beclouds the eyes of otherwise capable scientists, so that what was found written in a book long ago has become the gospel from on high. Thus, several of the members of your panel have failed completely to see this very clear problem associated with lead in the environment of man. For example, the man who wrote Chapter4F missed this point completely, in failing to recognize the two fundamental types of exposure.

This brings me to refer to an experiment which I know about, simply because it represents a means of investigating, directly, the tolerable concentration of lead in the air, which on continuous (or virtually continuous) exposure, is incapable of causing enough of an increase in the rate of the excretion of lead in the urine, or, later, an increase in the concentration of lead in the blood. I will not go into the details, here, but it was found that in the prison in Albany, the people in the University at Albany could set up an experiment (which I could not do here) in which a group of men could be subjected to exposure to the same kind of conditions to which our subjects had been subjected for 22 out of 24 hours per day for a period of weeks (by agreement with certain prisoners who were allowed to volunteer for the purpose, for what reward, I do not know). We worked on an increasing time schedule, and by extrapolation to 168 hours per week, undertook to find the tolerable level. For a number of reasons, the results were not entirely sharp and well-defined, but we suspected that 10 micrograms per cubic meter was near the tolerable level. To shorten the story, it appears that the experiment in Albany has definitely demonstrated that suc is not the case, but that 10 micrograms is too high. It is possible that 5 micrograms is satisfactory, and I wish to see this investigated without delay, for we desperately need the answer. I go to Albany on the 13th to talk with the group there and learn just what they have done. I expect to look carefully and critically into the manner of conducting this experiment, so as to find some flaw in it, if possible. Frankly, however, I do not expect to find such a flaw, although I will give it a very hard look, for I am disappointed at finding that our own method of research turned out to be fairly wide of the mark. I shall report to you what I learn, for your information and that of the panel, since this is a very crucial situation, about which you should know, in confidence, while you keep your own counsel and wait for a definitive result. The important thing to bear in mind, I think, is that this is one of the series of experiments in which we have been engaged for many years, to establish the facts in this specific manner. This industry is fully prepared to abide by these results without compulsion, but it does not appear that this will be the real reason for the abandonment or reduction in the use of lead antiknock compounds by our society. It seem that the automotive and petroleum industries have come to their own conclusions as to what is wise for them to do, in their own interests without knowing the truth about the issue of human health. I say this not resentfully, but rather somewhat sadly, for

if this is the way in which our society goes about problems of environmental health, we are in for trouble.

Now, as to the two of your documents which I am returning to you, and as to my role in this matter, I have a few comments to make. First of all, I have made every effort to confine my comments and criticisms to the areas which relate to my knowledge and experience. I know, at second hand, about much of the other material, but I do not set my judgment up against that of technical people in the areas concerned.

Second, there are errors of fact and of judgment in the two manuscripts referred to, and there are ambiguous and incomplete statements here and there. I have commented on these matters and have hand-written my comments into the manuscripts or their margins. There are other matters of opinion which are not justified by the available evidence, particularly in the recommendations. I have commented on the latter and have indicated what I consider to be of some importance in these matters. Here are matters of opinion and of judgment, and there may well be disagreements. I assume, of course, that your people will act and think and decide as they choose, but I consider it wise to choose carefully what to do and how to do it, for the very simple reason that there are very many matters that require research in this and other fields, and it will not be possible to finance all of these experiments. Moreover, if, as I believe, lead antiknocks are to be phased out of existence during the next 5 to 10 years, funds simply will not be available for much work on these projects, and those of us who expect to continue our work through private or public funding, for other reasons than those related to this specific environmental problem, will be having a difficult time in designing experiments which will relate to existing problems of human health. I would add to this the fact that I would hesitate to embark on any elaborate program of experimentation in this field, based upon the results obtained by the exposure of rats. The things I want most to know, quantitatively, cannot be found out by such means.

I am sorry not to have time to cover this entire report in its second draft. However, my opinions on parts of it are not worth very much, and I am committed to an editorial job of some size which must be completed by a certain date, which is beginning to loom up threateningly. I simply must not allow too many other things to interfere with it any longer. I trust that what I have been able to do will have been of some service to the group.

Sincerely yours,

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

RAK:wb

NATIONAL RESEARCH COUNCIL

NATIONAL ACADEMY OF SCIENCES NATIONAL ACADEMY OF ENGINEERING

2101 CONSTITUTION AVENUE WASHINGTON, D.C. 20418

DIVISION OF MEDICAL SCIENCES

MEMORANDUM 31 March 1971

To: Members, Committee on Biologic Effects of Atmospheric Pollutants, and Reviewers

Via: Dr. T. D. Boaz, Jr.

From: L. H. Marshall, Ph.D., for Panel on Lead

Enclosed please find the SECOND DRAFT of Airborne Lead in Perspective. Chapters 2 (Lead and Plants) and 5 (Biologic Effects in Domestic and Wild Animals) have been omitted* because they have not changed substantially from the first draft. Chapters 1 and 3 have been rewritten, and Chapters 4, 6, 7, and 8 and the Appendices are new.

This draft has not yet been to our literary editor, nor have the references been verified and collated; the art work is in preparation. Most of the data in this draft were presented in the first draft, but their manner of presentation has been improved. We would appreciate at this time your looking at the draft from the point of view of completeness and coherence. Chapter 8 (Conclusions and Recommendations) should be especially scrutinized for we need to know if the data justify the conclusions.

The third draft is scheduled for distribution in three weeks, so that comments to be effective must be received by April 15. My phone is 202-961-1805 if a call is more convenient than writing, or you may wish to get in touch with the Panel's Associate Editor, Bertram Dinman (313-764-5476) or the Chairman, Paul Hammond (612-373-0816).

LHM/th
Attachments

*These chapters are included for Drs. Baetjer, Meier, Lilienfeld, and Bacon because they did not receive them previously.

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