

UNIVERSITY OF CINCINNATI
COLLEGE OF MEDICINE
DEPARTMENT OF ENVIRONMENTAL HEALTH

KETTERING LABORATORY
EDEN AND BETHESDA AVENUES
CINCINNATI, OHIO 45219

April 3, 1967

Mr. Victor Sussman
Air Pollution Control Committee
P.O. Box #90
Harrisburg, Pennsylvania 17120

Dear Mr. Sussman:

Your letter of March 20, indicating that the official record of the hearing of January 19, with its supplement, had been closed before the receipt of my letter of March 13, together with an additional item noted in a transcript of the record, have combined to give me the impression that my position in professional circles and before the public, and even before the Air Pollution Commission and the Council of Technical Advisors, may be somewhat less than enviable, for reasons which will appear in my further comments. Accordingly, I have come to the conclusion that I should address myself further in a letter to you, in an effort to clarify my position in the minds of those most concerned with the record, and to forward copies of the letter to all members of the Commission and to the Chairman of the Council.

My appearance at the hearing on January 19 requires no explanation beyond those given in my statement, except perhaps for the comment that I was there at your invitation to discuss certain matters of fact concerning the current status and the outcome of some experimental work under way in the Kettering Laboratory, and to give such advice as I believed to be pertinent. The experimental work under consideration was designed to provide information on which valid criteria concerning a tolerable concentration of lead in the ambient atmosphere, in relation to public safety, might be made available. A further matter of special significance had need to be clarified, since certain published data from the Kettering Laboratory had been drawn upon by yourself to formulate a standard proposed for adoption by the Commonwealth of Pennsylvania. The data in question had not been intended for this purpose, having been recognized as incomplete, and I was put to the necessity of pointing out a flaw in their unmodified use in a calculation on which a standard was based. I had never undertaken previously to give a precise number to this factor, but being called upon, so to speak, to introduce a numerical correction into your calculation, I did so according to the most reliable information available, and came out, in the same calculation, with eighteen micrograms as the hypothetical standard, instead of five which was the result of your calculation. I implied, no doubt, that this was a better basis for a standard than that which had been chosen, but I rejected both numbers in preference to a range, which would be based on experimental evidence rather than hypothesis. My view of the promulgation of a standard for the ambient air at this time, is that such action is premature, until such evidence has come to be available.

In the latter connection, it may be pertinent to mention the fact that at least two convocations of professional personnel, both called by national professional organizations, and also one State health agency - The Department

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of Public Health of the State of California - have examined the available facts concerning various standards of air quality that might usefully be established, including that for lead, and have concluded that the information concerning lead, while nearing a satisfactory state, was not yet adequate.

In the interest of brevity, I confined my remarks at the Pennsylvania hearing to matters of seemingly immediate relevance, on the basis of the near completeness of the public record elsewhere - that of the hearing before Senator Muskie's Committee in Washington, D.C. in 1966 - of all of the pertinent information from the Kettering Laboratory on the occurrence and significance of lead in the environment of man, including that in the ambient atmosphere.

It should be noted also, that the source of almost all of the pertinent information on this subject, as revealed at the Muskie hearing and the Symposium On Environmental Lead Contamination sponsored by the Public Health Service in December 1965, was the Kettering Laboratory, with the exception of Public Health Service Publication No. 999-AP-12, of January 1965, entitled a Survey of Lead in the Atmosphere of Three Urban Communities. (This survey served to extend and to confirm the results of previous surveys of the Kettering Laboratory.) It was for this reason that I was pleased but, at the same time, obliged to accept your invitation to appear at the Pennsylvania hearing to offer such information and advice as might be useful to yourself and your associates.

Since the date of the hearing, the letters of three prominent physicians, Katharine Boucot Sturgis, M.D., John R. Goldsmith, M.D., and Harriet Hardy, M.D. have been directed to your attention, in implied or outright criticism of my statements and advice. Despite the fact that none of these spokesmen of a different viewpoint appeared at the hearing, their letters appear in the supplement to the record of the hearing. You were most considerate in giving me the opportunity to comment on two of these letters, but my comments do not appear in the record. The third letter, Dr. Hardy's, in some respects the most critical of the three, I did not see until I examined a transcript of the record. (I do not suggest that you were at fault or that you intended to by-pass me, for I know something of how these matters come out.) In consequence, I may be said (if in no other than a formal sense) to be standing silent, against the weight of three counteropinions, and certainly I would seem to be outweighed numerically in the record.

In view of the fact that two of my critics (Drs. Sturgis and Hardy) have had no experience in the actual examination of the people and the situations involved in this putative hazard, and that only one (Dr. Goldsmith) has direct responsibility for judgments in relation to public safety in this area, I am in no sense actually outweighed as to judgment, and I cannot accept in silence any such appearances. For this reason, I am going beyond the writing of the letter concerning the nature of the views of Drs. Sturgis and Goldsmith, and am commenting in some detail on Dr. Hardy's letter and the publication submitted with it. In addition, I am briefing my remarks concerning the other two letters, thereby supplementing this letter for the benefit of your Commission and Council, to whom, in due course, I shall forward copies of the original letter.

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I should like you to know that I do this, not out of any doubt that you will inform all of those referred to above, as to what has transpired, but rather because I have a professional responsibility to speak for myself, and to leave no stone unturned which will enable you, your associates, and your sovereign Commonwealth to be possessed of the available information whereby you can arrive at a decision that will be satisfactory in your own eyes and also in those of the sister States and of the professional world, in days and years to come. The establishment of the precedent in this matter is of serious and significant moment to many people, not the least to yourselves. It would be well, in the professional sense, if the decision were to be postponed until it can be firmly established on valid evidence. If, out of practical urgency, it cannot be postponed, it should be as nearly correct as the present weight of evidence will permit, rather than upon the dubious weight of a voice-vote.

This brings me to the consideration of the letter of Dr. Harriet Hardy, and to a critique of the contents of a reprinted article prepared by herself and published in Clinical Pharmacology and Therapeutics, under the title "What Is The Status of Knowledge of The Toxic Effect of Lead On Identifiable Groups In The Population?" I believe that something needs to be said about both the letter and the views expressed in the reprint, as they are intended to relate to the present and ultimate tolerable concentration of lead in the ambient air to which the human population is exposed.

First, let me say that I have little quarrel with Dr. Hardy in this instance, so long as she sticks to clinical lead poisoning and the consequences of such poisoning in the immediate and remote future of the victim. There is room here for certain differences in opinion, as to points of view based on experience, and in the degrees of emphasis to be placed on various aspects of the matter, but there is no serious disagreement as to the main facts, as differentiated from their interpretation. Whereas the first episode of lead poisoning, in the adult, is usually a comparatively brief and largely self-limited disease, without recurrence or sequelae, if the exposure that induced it is discontinued or reduced appropriately, there are seriously and even permanently disabling cases, and also fatal cases, especially among children. It may be that in children there is some factor(s) of intolerance, but the fatalities, as I have had occasion to know through the investigation of a fairly large series of cases from 1930 to the present time, are associated with extraordinarily high dosage. Otherwise, few vital questions about clinical lead poisoning arise to promote controversy. In the course of some forty years of practice, relating especially to lead hazards, I have seen, through my own eyes or, in later years, through those of competent clinicians who have worked directly with me and our team of engineers and chemists, more cases and more types of cases of lead poisoning, in all likelihood, than any other person in the United States. Our group has investigated many people employed in a wide variety of lead-using industries, and a large number of persons in the community in general. Many actual and alleged cases of lead poisoning have been referred to us from various sources over the years. We have also studied carefully, both clinically and analytically, several hundred occupational groups subjected to minimal, safe, and dangerous levels of exposure to lead. It seems a bit odd, therefore, that Dr. Hardy should object to my testimony at your hearing as being based only on the behavior

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of "healthy young men." The experiments on which I reported there had in their background my total clinical and experimental experience in the field, but were designed to answer one specific question, namely, how much lead in the air and elsewhere can healthy young men handle without evidence of an elevation of the rate of their excretion of lead in the urine, or increase in the concentration of lead in their blood. No one else has attempted to answer this question, and therefore it deserved primary consideration. I drew on my entire experience, however, to give you and your associates the substance of my best judgment. This is not to suggest that my judgment necessarily stands alone and unquestioned against all divergent opinions, but it does stand alone in the present company of my critics for the evidence which gives it support. The situation represents long experience and an accumulation of evidence, admittedly incomplete in some respects, over the years, as opposed to supposition and inference. If this is a seemingly immodest statement, I submit that it is nevertheless a simple statement of fact, which ought to be recognized as such.

Now as to the substance of Dr. Hardy's published article, most of the facts assembled in it from the literature are not especially controversial. One can easily criticize some of the conclusions of some of the authorities cited, and even go further and make certain alternative suggestions as to certain interpretations of their observations. The weakness of the evidence submitted, however, is not that it is incorrect, in itself, but rather that it is irrelevant. No informed person, so far as I know, denies that a small child with a large intake of lead is in serious danger. Here is a matter of quantity. No small child can avoid or has ever avoided the ingestion and inhalation of lead, in small quantities, no matter when or where on this planet he has been born and reared. The question is how small. It is nothing short of impertinent to talk about serious danger in this connection against the evidence of the centuries, unless quantitative considerations, at least as to orders of magnitude of lead absorbed now and in the past, are brought into the discussion.

No one denies that a pregnant woman, in an hazardous (occupational or other) environment, is in danger for herself and her child. But again, all pregnant women have been ingesting and inhaling lead on this planet for centuries. Illness due to lead derives from unusual types and degrees of exposure to and absorption of lead, rather than from exposure to the usual environmental conditions of our time.

No one doubts that the person who has been subjected to the absorption of admittedly dangerous quantities of lead over a long period of time is in jeopardy at that time and possibly for a long time to come. It may be that chronic disease of the kidneys is induced by such exposure to lead. The evidence for this, in my opinion, is dubious, but several men whose opinions I respect are convinced of the fact. Regardless of where the truth lies, this controversy has no remote relationship to the prospect of renal damage from the absorption of traces of lead.

Infants and children may be especially vulnerable; pregnant women, with the future generation of mankind at hazard, may be especially vulnerable; the sick,

infirm and physiologically impaired persons in the population may be especially vulnerable; perhaps, but I doubt it, the aged, per se, may be especially vulnerable. Vulnerable to what? To a toxic dose of lead, certainly. But to a dose that is toxic for them only? If so, what is the dose? If one applies the known facts, the existing margin of safety based on physiological considerations is relatively large and yields little suggestion of risk. The intake of lead from all sources - food and beverages and the general atmosphere, under ordinary conditions, ranges from about 0.14 to 0.36 mg. per day, on the average, resulting in the daily absorption of as little as 0.025 mg. (25 micrograms) to as much perhaps as 0.075 mg. (75 micrograms) per day. Under these conditions the range of the concentration of lead in the urine, on the average, extends from about 0.015 to about 0.034 mg. per liter, while that in the blood extends from 0.01 to 0.03 mg. per 100 grams. (Individual values run somewhat higher at times because of daily physiological variations and, more importantly, analytical deviations.)

In contrast to the numbers cited above, the conditions associated with the absorption of potentially dangerous quantities of lead are characterized by gross differences in the average concentration of lead in the urine and blood. Thus, the lowest level of the concentration of lead excreted daily in the urine of the person with lead poisoning is 0.15 mg. per liter, while that in the large proportion of cases is in excess of 0.20 mg. per liter, running up to 0.30, 0.40 or 0.60 mg. per liter. Likewise, the lowest concentration of lead in the blood in the person with lead poisoning (at the onset) is 0.08, while in most of the cases, the range extends upward, to as high as 0.7 mg. per 100 grams. These differences appear to the novice to be small, but they have a somewhat different complexion, when one reckons with the time factor in the absorption of lead. For example, when one administers lead by mouth in the dosage of 2 mg. per day, in solution, with meals, approximately 300 micrograms are absorbed daily above that absorbed under ordinary conditions. This absorption of lead daily over the period of two years results in an increase of about 0.09 mg. per liter in the urine, and of about 0.04 in the blood, the concentration at this time in urine and blood being 0.115 mg. per liter in the former and 0.062 mg. per 100 grams in the latter. Lead poisoning has never been known, in our experience, to occur in association with such findings as these, and yet, while the absolute quantities of lead involved are small, the increases above the usual or "normal" levels are of the order of 350 percent in the urine and 100 percent in the blood.

Another basis for comparison is equally revealing. Whereas the "normal" child of three years of age is found to have lead in his body to the extent of 40 to 60 milligrams, the quantities found in the poisoned child range commonly from ten to twenty times these amounts and at times may be of the order of thirty times. These are not hairsbreadth differences, but are in fact in different universes of phenomena. That such is the environmental situation of man in this country at this time, in the matter of the lead content of food, beverages and the ambient air, appears to have been demonstrated, if not with absolute certainty, then with every reasonable probability, based upon the precision of balance experiments and on the profusion of "spot" observations on many persons in the general population. Critique here should be concerned

with the few loopholes in this evidence which are yet to be plugged. But such is not the case. Rather, the discussion has centered around the effects of lead, not in the low level of its customary intake and absorption by persons in our general population, but in the totally different range of intake and absorption which historically has induced lead poisoning. Lead poisoning has not been found to be induced by the absorption of "traces" of lead. Quite to the contrary, it is induced by the absorption of lead from an environment which can be defined in quantitative terms (as represented by a range of dosage) as dangerous. The principle here, with respect to dosage, is hard for the physiologically naive person to accept with complete confidence, although it is virtually universal in its application to degrees of stress as applied to vegetable and animal life. It is doubly hard perhaps, for the clinician, with his (or her) awareness of the tradition and history of lead as a poison, and his having confirmed the tradition through his own experience, to think effectively and realistically, in quantitative terms, of lead as an inevitable and harmless, perhaps even useful, constituent of living things in quantities of a slight order of magnitude, as against lead as a poison in a much larger order of magnitude. But such is the very substance of physiology, and the problem, from the aspect of human health, is to know, in quantitative terms (with a reasonable margin for error in the intervening area), the limits of the ranges of harmlessness and toxicity.

No one can maintain, at this point in time, that the limits referred to above have been defined precisely for all men in all conditions of life. No one, least of all an objective scientist, should doubt, however, that they have been defined with reasonably satisfactory accuracy, in relation to present conditions, and that they can be rendered more precise in the near future, so that we may face the issue of tomorrow's changed conditions with equanimity. It can be and has been said, with justice, that no comparable problem of environmental health in the United States has been examined more intensely, and with greater assurance of the validity of the findings, than has this one. There is no present reason for apprehension as to any potential hazard to human health that might be represented by lead in the general (or ambient) air in the prevalent levels of concentration. Moreover, the question of the tolerable level of concentration, beyond which some degree of risk may arise, is susceptible of determination in the practical terms of human physiology, and is on the point of being determined. Meanwhile, if for any reason, some level of tolerance must be advocated or adopted, it should be based on the best available physiological evidence rather than upon irrelevant considerations of the nature of the disease, lead poisoning, which certainly arises out of a quantitatively different set of environmental condition that those under discussion in relation to the ambient air.

In supplement to the preceding paragraphs, I should like to add a few words as to the substance of my comments on the letters of Katharine Boucot Sturgis, M.D. and John R. Goldsmith, M.D.

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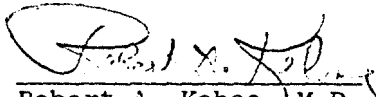
While acknowledging the competence of Dr. Sturgis in her own field, I do not consider, nor will she claim, that such competence extends into the field of toxicology, generally, nor specifically into that of the behavior of trace metals in men in relation to health and disease. Her support of the standard of 5 micrograms of lead per cubic meter in the ambient air has no more basis in judgment than that it was settled upon originally by the appropriate authorities in the Commonwealth of Pennsylvania, and that she felt that I was taking exception to it on dubious grounds.

As to the views of Dr. Goldsmith, I expressed the opinion that he was giving much too much weight to slight differences - differences within the range of variability due to fortuitous or unrecognizable variables, and was arriving at unwarranted conclusions through the application of precise mathematical treatment to insufficiently precise data.

It should be said, in addition, that much too much credence has been given to the likelihood that the absorption of lead in trace quantities (such as those that are involved under present environmental conditions) may induce injurious effects that are not included within the presently recognized syndromes of lead poisoning. It is as though one should conclude that because lead is injurious within certain limits of dosage, it must be somewhat injurious in much lower dosage, and that the clinician has simply lacked the knowledge and skill required to detect such injury.

I regret that such seemingly lengthy comments are required to bring the facts into focus in this situation, but the subject has been shrouded in somewhat unrealistic complexities which need to be untangled.

Sincerely yours,


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

RAK:wp

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