Lead Industries Association

60 EAST 42ND STREET

NEW YORK 17, N.Y.

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DIRECTOR OF HEALTH AND SAFETY

July 21st, 1958

Robert A. Kehoe, M. D., Director
Kettering Laboratory of Applied Physiology,
University of Cincinnati,
College of Medicine,
Eden Avenue,
Cincinnati 19, Ohio.

Dear Bob:

I need not explain this delayed word of thanks for your exhaustive and interesting letter of July 3rd. It was in the stack on my desk when I returned last week from a four weeks absence (in the course of which there were relaxing reunions with Alice Hamilton at Washington, Paul at Salt Lake, Red at San Francisco, and Tom at Santa Fe), and I only now have had the time to absorb all that you have said.

I don't know whether you recall Paul's famous "Abraham Lincoln story," having to do with correct observations and erroneous deductions, but portions of Moeschlin's paper seem the perfect example of this combination.

Even though it dates back some seven years (a long time for one with my forgettery), I well remember the walnut shell matter. How anyone could confuse the hazard here involved with that alleged to inhere in leaded exhaust gases is quite beyond me.

I have been much interested to note the increasing conservativism anent EDTA, of which Harriet Hardy's attitude is an outstanding example. My own thinking has undergone a similar revision, so this suits me fine.

You say that you have no knowledge of the Swiss version of this product. I have a single amoule, labeled "Calcium Hausmann," and could probably get more from the same source if it were wanted. I once asked Hervey Elkins if he thought an analysis of this would be profitable, and he was not enthusiastic. However, if you think otherwise, I would be glad to see what I can scare up for you.

It is fortunate that the German for "rat" is "Ratte". Otherwise, I fear that the Herr Geheimrath (of whose divinity I am well aware) might take serious exception to your omission of his terminal "h".

Knowing that it will interest them, and feeling sure that you will have no objection, I am sending copies of your letter to the Boston pals to whom I am indebted for the Moeschlin manuscript.

MB:cm
enclosures
Postscript - 2

Sincerely,

P. S. By way of codicil, here is a copy of Moeschlin's reply to the letter from Brugsch of which I sent you a copy.

MB

June 3, 1958

Solothurn, May 24, 1958

Dear Dr. Brugsch:

Many thanks for your letter of May 15, 1958 which interested me very much. In answer to your question, I can tell you that since my publication in the Schweiz. Med. Wschr., August, 1957, four additional cases which terminated fatally have been reported to me, due to kidney damage in the course of Ca-EDTA treatment a severe nephrosis occurred with fatal termination. One case was reported to me from Zagreb, Yugoslavia; one from Germany; and two additional cases from Switzerland. Five cases altogether are known to Suval at Lucerne.

I really believe that one has to be very careful. We are now carrying on extensive clinical investigations which will be published later, in which we further experimented with various dosages on all sorts of patients with severe Cancers and other diseases. It has become apparent that if one reduces the dosage to 20 mg./kg body weight, kidney damage is not observed, as for instance, with a dosage of 1.2 g. daily for a patient weighing 60 kg., when we gave it for three days and then interposed a treatment free period for three days. Perorally the drug, while less effective, is better tolerated, and one is justified to increase the dosage to 30 mg./kg., in other words, again a total of 2g. perorally. I believe, however, that 2 g. intravenous per day is perhaps somewhat too dangerous and particularly if 4 g. i.v. are given as previously has been stated by American authors that in certain cases a fatal complication could occur. I am enclosing below a copy of our therapeutic schemes as worked out by us for the physicians in Switzerland.

Ca-Sodium EDTA (Ca-Versenate) Ion exchange
(1 Ampule Calcium Hausmann forte = 2.4 g Versenate - 250 mg. Ca)

Dosage: a) i.v. : not more than 20 mg. Versenate per kg. body weight.:
(for instance, 60 kg. patient = 1.2 = ½ Ampule in 500 ccm 5% Glucose or Laevulose, drop infusion)

b) peroral: Adults 2 g. daily permitted
Children 30 mg./kg. body weight per day.

Duration: Three days therapy, three days intermission, then repeat according to clinical picture, in 5-10 Courses.

Urine Control: In the presence of 2+ albumin, stop immediately!
In the presence of pre-existing renal damage, be careful!! One-half dosage.

Looking forward to hearing from you again later on, I remain,

With best regards,

(Signed) S. Moeschlin

July 3, 1958

Mr. Manfred Bowditch
Lead Industries Association
60 East 42nd Street
New York 17, New York

Dear Manfred:

I return to you herewith the typed and the Thermofax copy of Brugsch's translation of Moeschlin's paper on lead intoxication. I am grateful to both you and Brugsch for your respective contributions to my information. I was somewhat familiar with Moeschlin's paper because of a series of discourses sent along to me by another Swiss physician, R. Fatzer, who has needled me, from time to time, as the arch-enemy of Switzerland in having denied the hazard of the distribution and use of leaded gasoline. In Fatzer's eyes the cases described by Moeschlin were more important for having proved me wrong about this lead hazard than they were for their demonstration of the bad effects of calcium versenate. Several Swiss physicians, still under the influence of Zanger, now deceased, who wrote on this subject out of no knowledge at all, in 1923, and was responsible for having lead/gasoline banned from Switzerland, have taken on this battle. When the ban was lifted temporarily during the war, and then this action was sustained after the war, there was a storm of protest from several sources. It died down to some extent, but has persisted in spots. Professor Zanger was regarded as the great authority on such hygienic matters, and as you know, the Herr Geheimrath Professor speaks with the voice of God and is never wrong. I have visited Switzerland three times to discuss this matter with the authorities and have been consulted by them here, and I talked twice with Zanger, who was prepared to alter his views somewhat, but not his pronouncement. This is a long story into which I cannot go here. I can only say that you could have no idea of the emotional content of this battle in certain medical circles in Switzerland unless you had been involved in it.

Now as to Moeschlin's cases of lead poisoning, I am prepared to accept their validity, but let me call your attention to the important fact that these have nothing to do with the problem of the contamination of the urban atmosphere with exhaust gas containing lead. The pertinent cases involved exposure to the deposits within the internal combustion engine. When these are removed by dry or hot methods, the lead content of the air in the immediate vicinity is contaminated with finely divided carbon and finely divided inorganic lead compounds (the chlorbromide, sulfate, phosphate and carbonate, usually in variable proportions dependent upon the precise nature of the fuel and the fuel additives). I called attention to the problem of the garage mechanic years ago, and within the industry I have done everything I could, when mechanics worked more or less continually at this job in handling fleets of cars, to surround this operation with suitable

precautions. You will remember, perhaps, that with the introduction of an unventilated machine to blast out the carbon of motors with nut shell or other abrasive material, there was a series of cases of lead poisoning, which led to a new design of the equipment with suitable ventilation. When a mechanic does this job occasionally by ordinary means, he never gets into trouble, but if the circumstances are such that he incurs daily exposure to lead for some hours in this work, cases of poisoning occur. This can be prevented, and in general it has been prevented in the establishments where fleets of cars are dealt with.

I call your attention also to the fact, which we pointed out years ago, that the garage mechanic sustains other types of exposure to lead in relatively small quantities, generally. He does a bit of soldering; he removes paint (the undercoats of which are high in their lead content) from cars, and repaints them from time to time; he smooths fenders and car bodies with molten lead alloy by grinding the cooled metal to a nice even surface; he handles and sometimes repairs storage batteries. These things, in the average repair garage, result in some absorption of lead, and undoubtedly, the exhaust gas in the repair garage is often high in concentration. The total effect is to differentiate garage mechanics, as a class, from the handlers and users of leaded gasoline, by reason of a barely significant increase in the mean level of their urinary lead excretion, and by a somewhat less pronounced increase in the lead concentration in their blood (the urinary value is about 0.05 mg. per liter in comparison with about 0.03 mg. per liter for ordinary persons with no occupational lead exposure; the blood value, barely significant statistically and only so because of the large number of observations, is about 0.038 as differentiated from the normal level which is slightly under 0.03 mg. per 100 grams). And yet the garage mechanic rarely reaches the level of dangerous lead absorption and almost never has lead poisoning. With the exception of the rare man of this type whose regular job involves some special type of exposure to lead, the garage mechanic is not involved in a lead hazard in his occupation, because most of his jobs do not result in any significant exposure.

I shall not go into the quantitative aspects of the exposure of the urban population, and some of its special groups, such as parking garage attendants and traffic policemen, to lead from the exhausts of automobiles. This is a very long story, on which, as you know, we have worked for many years. Suffice it to say that this problem, for a number of good quantitative reasons, is of greater importance in the USA than elsewhere; that we have investigated it extensively from the two aspects of (1) the lead content of the atmosphere, and (2) the evidences of lead absorption on the part of exposed persons; that we have good, sound data on both sides, and in addition we have studied and are continuing to study the fate of inhaled lead (as we did ingested lead, earlier) so as to establish physiological standards of safety.

The foregoing matters will not be news to you, except perhaps as to their scope, but I speak of them to set the record straight. Our friends in Switzerland, including Moeschlin, are talking about lead exposure in non-quantitative terms, and are discussing the lead metabolism in the terms of the early nineteen twenties. I suspect that Moeschlin is a fairly good clinician. He may even be a brilliant one, but like most European doctors, he mixes observation with interpretation to the point where it is difficult to differentiate one from the other, and while he does not confuse the issues completely, he talks about exposure to tetraethyl lead in connection with the work of a garage mechanic, apparently without recognizing that the overwhelming proportion of the lead with which these men are concerned in a motor is only an inorganic, thermal decomposition product of tetraethyl lead. The evaporationof gasoline spilled or leaked on a hot engine is almost negligible, while the tetraethyl lead which escapes from the "breather," as well as the carburetion system, is of such little moment as to be hard to detect. The lead deposits within the engine, on the other hand, dependent upon their total quantity and the time at which they are being removed, may contain grams of lead along with more grams of caked carbon. It is this failure to explore the facts and the glib theorization about the sources of lead exposure without having the facts, that frustrate me. We are all guilty of this to some extent in the practice of clinical medicine, but one would suspect that we could learn its perils, and be cautious in our writing.

The clinical descriptions given by Moeschlin are not those of tetraethyl lead poisoning, and it is apparent that he has never had experience with tetraethyl lead poisoning. If his analytical findings are to be trusted, these are sufficient to prove this point, since the concentration of lead in the blood in tetraethyl lead poisoning is never increased more than slightly, whereas in his cases the blood levels were in the range associated with the absorption of dangerous quantities of inorganic lead.

Now as to the significance of the outcome of these cases in relation to the use of calcium versenate, I am not in position to question Moeschlin's conclusions. Two of the cases seem to me to point to the correctness of his interpretation. Two points, however, need to be made. The most important of these relates to the dosage of the agent, which by our standards was high. I believe I would be much more cautious in my use of it. It has been demonstrated that low dosages will accomplish much of the desired purpose, and moreover, we, here, have had no trouble at all since the first two serious cases (children in very bad condition) appeared to respond badly to this therapy.

The other point relates to the preparation used (the calcium salt along) with which I have had no experience. It may be just as good as the disodium calcium preparation. I have no good reason to doubt the satisfactory quality of the Swiss preparation but, on the other hand, I have no knowledge of it.

In any case, Moeschlin has gone to the extreme, I think, in denouncing the use

of versene altogether. That it should be used with care, and that its use had best be avoided, in certain cases, seems reasonable. Certainly American experience as thus far reported, does not support this opinion. You will recognize, I believe, that I have not been one of the great enthusiasts for this form of therapy, largely because it accomplishes but little more than seems to be accomplished by nature in a little longer time. I believe it to be advantageous in the treatment of the often disastrous lead intoxication of early childhood, which is really its crucial test. There is, however, no evidence that it saves lives. It appears to shorten the illness, and so is advantageous, especially, since it seems not, of itself, to be dangerous when used with appropriate caution.

There is one other aspect of this matter which I am sure you would expect me to mention - namely, the relationship of these observations to the indiscriminate use of disodium-calcium versenate in lead poisoning and in the hastening of the lead excretion of persons whose exposure to lead may be potentially or actually dangerous. Since this is being done in this country with little or no medical supervision, it seems likely that we are indulging in a dangerous, as well as a foolish and immoral, practice.

I think I have spent enough of my day on these comments, and I'd better get to work elsewhere. I hope they convey my views reasonably well.

Sincerely yours,

Robert A. Kehoe, M. D.

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