April 14, 1960

Wm. Gordon Pauley, M.D.
3, Palm Lane
Levittown, Pa.

Dear Doctor Pauley:

I hasten to reply to your letter of April 7th before I get bogged down in other work and find a week or two hence that I have not replied to it. Since this is destined to be the chronic state of my correspondence, generally, for some months to come, I must make an occasional exception in matters of special interest.

Let me dispose of your question #2 first by saying that if you are referring to the article which I wrote for the last edition of Cecil's Text of Medicine, I can add little to it. In this article, however, I dealt only meagerly with industrial hygiene. Rather, I was writing mostly for the physician in private practice who has little understanding of the industrial problem, and, as a rule, little real interest in it.

The other questions require more comment, and indeed, much more than I can take time to give in a letter. I shall take them in sequence, however, as briefly as possible. Let me say first, however, that "deleading" of any kind, is not a prophylactic procedure of industrial hygiene. There is only one way to deal with hazardous industrial exposure to lead - namely, by bringing it under adequate control by engineering means. There is no substitute for this, and unless the industrial physician makes this clear to the responsible people in industry, he is doing them a disservice.

1. Disodium Calcium Versenate administered orally is not a "deleading" agent at all under most circumstances, and is certainly not an effective agent when given in this manner. The evidence indicates that it promotes the absorption of lead in the alimentary tract, and that a part of this absorbed lead is responsible for the elevation of the concentration and output in the urine. Instead of being an advantage it is probably the reverse, but in any case the benefit is very slight. As a prophylactic measure it is ineffectual and is also based on the wrong principle. Prophylaxis consists in (1) the control of the environmental exposure within safe limits, and (2) the removal of men from hazardous exposure as soon as they have reached the threshold of a dangerous degree of absorption of lead.

3. Men should be removed from an occupation in which they incur potentially dangerous exposure before any symptoms of illness (including abnormal levels of porphyrinuria) can develop and as soon as the

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level of lead concentration in the blood exceeds 0.07 mg. per 100 grams of whole blood. (There is a threshold value of comparable significance in the urine, but this cannot be determined for the individual except by multiple analyses, since the analytical result on a single sample of urine is not sufficiently indicative of the general rate of the urinary excretion of lead. The blood varies little and hence is more indicative of the status of the individual.)

Men can remain at work with the assurance of freedom from lead intoxication so long as the blood level is below 0.08 mg. per 100 g. The best methods of analysis, however, yield reproducible results only within the limits of ± 0.01 mg. per 100 grams, and, therefore, a single result of 0.07 may in fact be as high as 0.08. Thus anything in excess of 0.07 may be indicative of danger. For this reason we obtain and analyse duplicate samples. Men who continue to work after reaching the threshold level are ready candidates for lead intoxication if their exposure should be increased suddenly or accidently.

4. Nothing (absolutely nothing) is known of the mechanism of exciting lead intoxication. We have looked at this in a variety of ways, and we suspect that loosely bound lead is converted to ionized lead, but there is no proof and such proof would be very difficult to obtain.

5. I do not think that porphyria has anything to do with lead colic. I regard the increase of the porphyrins in the tissues and urine to be the result of an interference with the final steps in the metabolism of hemoglobin; when it is induced by lead it is an indication of intoxication, at which time a common manifestation is also colic. The two occur simultaneously but in no other relation, so far as I can see.

With respect to your reference to the Lead Information Center, I am gratified by the productive interest shown by several of our colleagues in pediatrics. For many years we/had, as do all of the older American cities, a serious problem of lead poisoning in children. It has taken time to bring the problem to the point of community action, but at long last we have reached that point.

I find I have neglected to point out the principal shortcoming of the use of "Versene" for deleading. This chelating agent has virtually no direct influence on the lead in the skeleton (in which 85 to 95 per cent of the lead in the body is usually found. It combines with the lead in the soft tissues and the chelated lead is excreted at an increased rate in the urine. However, whereas the patient may lose 10, 20 or 30 milligrams of lead in the urine in the course of a 5-day round of intravenous therapy, there are still hundreds of milligrams in the skeleton. After the lead has escaped from the soft tissues, the equilibrium between these and the skeleton is disturbed, and lead is lost from the skeleton to the soft tissues. Again 10, 20 or 30 milligrams may be available for excretion/if another course of intravenous therapy is instituted. And so this can go on for several rounds of therapy until the further loss of lead from the skeleton is too slow to greatly elevate the lead content of the soft tissues. At

this point this therapy has accomplished all it can do. You can see, therefore, that the common concept of rapid deleading is incorrect in the quantitative sense. Every patient who develops lead poisoning as the result of prolonged occupational exposure (i.e. many months, but not necessarily many years) has absorbed hundreds of milligrams of lead. The removal of but a small proportion of this may relieve symptoms (although it does not always do so effectively), but the large proportion still remains in the body to redistribute itself and to restore the high levels of concentration in the soft tissues.

The evidence behind these statements is voluminous, and I cannot even refer to it here. Such evidence is sufficient, however, to support the statements made. These statements do not cover the entire field, but perhaps they will serve to show that this matter is not so simple as many persons believe it to be.

Sincerely yours,

Robert A. Kehoe, M. D.

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April 14,

you can see, incorrect in coming as but

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April 7, 1960

Dr. Robert A. Kehoe
c/o Kettering Laboratory
University of Cincinnati
Cincinnati, Ohio

Re: Lead Intoxication

Dear Dr. Kehoe:

I read with interest the account of your city's Lead Information Center in the current J.A.M.A. and would appreciate any literature you have describing your program.

We are currently concerned with an industrial lead problem at Paterson Parchment Paper Company, Bristol, Pa. and would appreciate your comments on the following:

1. Efficacy of Calcium Versenate orally as a deleading agent.
2. Brief outline of your deleading program as it may differ from the conventional one as described in Cecil's Text of Medicine.
3. Whether you permit asymptomatic lead burners with elevated levels to remain on lead jobs even with stringent protective precautions.
4. What is known regarding trigger mechanism for inducing toxic symptoms in previously asymptomatic workers with elevated levels.
5. Comment on the possible relationship of lead-induced porphyria as a etiologic factor in the production of lead colic.

Congratulations to you and Dr. John E. Allen for the fine work you are doing in Cincinnati.

Sincerely yours,

Wm. Gordon Pauley MD.

WGP/bs

Wm. Gordon Pauley, M.D.