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July 16, 1964

Robert A. Kehoe, M.D.
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Eden Avenue
Cincinnati 19, Ohio

Dear Dr. Kehoe:

I regret that a rather heavy travel schedule in this last month has delayed my reply to your "courtesy" letter of June 4, 1964. Your letter relates to my printed answer of May 4, 1964 to the question of Lewis M. Grear, M.D. regarding "Laboratory Test for Lead Poisoning".

Several aspects of your letter of June 4th are sufficiently detailed so that it seems to me they may be profitably reviewed in reply.

We are in essential agreement (last paragraph, page 2 of your letter) regarding problems related to the accurate analysis of lead in blood and urine as they are faced by the practicing physician in this country. As the United States representative to the International Union of Pure and Applied Chemistry, Commission on Clinical Chemistry, as Chairman of the Education Committee of the American Association of Clinical Chemistry, as a practicing Clinical Chemist for many years and Fellow of the American Board of Clinical Chemistry I would fully endorse your view. You and I are in disagreement on this particular point with others in your own laboratory. I enclose for you a copy of a letter from M. R. Zavon, M.D. of the Kettering Laboratory who seems to take exception to my comment on the need for insuring that the analytical work be done in an adequately controlled laboratory. Recognition by the medical profession that chemical analyses should be conducted under the supervision of persons specifically trained in this specialty would go a long way toward insuring the kind of facilities and surroundings that would provide the stimulus required for top notch work on which you could rely.

No one can quarrel with your observations on the difficulties faced by the physician in the diagnosis of lead poisoning. The question posed in the Journal was not this one. It was rather on the subject of the analytical procedures which have been found helpful in establishing and verifying such a diagnosis. I think my printed reply was a reasonable answer to this question.

You have obviously not had an opportunity to include in your letter the experimental details on which you base your views concerning the essential similarity of the clinical results observed following exposure to lead under those conditions which are usually termed acute, aub-acute and chronic. For several reasons I am unwilling to accept your excathedra pronouncements on this subject.

The first reason is only of historic interest at this time. Some fifteen years ago I wrote a preliminary paper on the first application of Calcium EDTA for the enhancement of urinary lead excretion. In your review of the paper you suggested that a) your own work previously published has established that it was not possible to significantly increase the output of lead in humans carrying a high body burden of the metal and b) that the results reported by the authors were undoubtedly due to their inability to accurately analyse lead in urine. It has always been gratifying to us that our observations, made in those early years, have stood the test of time and that it is indeed possible by suitable chelating agents to induce an enhanced output of lead in the urine of humans. It is also somewhat amusing to us that our early conservatism on the correlation of enhanced lead excretion with any improvement in the clinical state of the patient has been echoed in these years by other investigators. Our additional experiences in developing modes of therapy for the removal of iron in vivo, for the control of calcium metabolism in vivo, and most recently for the enhancement of gold excretion in animals has not given me any reason to change my opinion that pronouncements from even so eminent an authority as yourself are subject to the crucible of experimental verification.

A second ground for differing with your views rests on experimental evidence concerning the disposition of exogenous metals in vivo. There are indeed differences in the rates and sites of deposition of metals introduced into the organism depending on the nature of the metal and the characteristics of the metal carrier. Likewise the dosage as well as the conditions of administration have some influence on the ultimate distribution of the compound. I am sure that you recognize that this subject is a complicated one. The same comment is applicable to the use of chelating agents as a provocative test to establish the body burden of various endogenous and exogenous metals.

It would be a great pleasure for me to discuss this subject with you in greater detail should opportunity permit. It happens that in the fall of this year I will be on sabatical leave from my post at the University. I would welcome an invitation to come to Cincinnati to review this subject in depth with you and your colleagues.

Most truly yours,

Martin Rubin

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May 21, 1964

Editor
Journal of the American Medical Association
535 North Dearborn Street
Chicago, Illinois

Dear Dr. Talbot:

On page 478 of the issue of May 4, 1964 the question is asked about the accuracy of laboratory tests for lead poisoning, and which tests are considered most accurate.

I believe that Dr. Rubin in answering, answered the question but may have been somewhat misleading in his answer. Obviously, the accuracy of all laboratory tests is "dependent on the availability of a well directed laboratory where competent studies can be done." With such a laboratory available, there should be no need for a provocative dose of a chelating drug or for any other laboratory determination other than the determination of the lead content of the blood and the urine. If there are symptoms indicative of lead poisoning and laboratory analysis indicates an elevated blood lead concentration, there should be no need for further confirmation. The presence or absence of stipple cells, elevated porphyrins, or other derangements of the normal become quite academic in the presence of symptoms and an elevated blood lead concentration.

Sincerely yours,

Mitchell R. Zavon, M.D.

MRZ/as