

November 23, 1964

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Dear Harriet:

Red Johnstone was kind enough to let me in on his recent correspondence with you over Calcium disodium EDTA, and I am impelled to quarrel with you, gently, about one part of your viewpoint concerning the usefulness of this chelating agent. As you know, I am not much impressed by its ability to alleviate symptoms of intoxication, but I am prepared to use it and to advocate its use for the accelerated elimination of lead from the soft tissues and, indirectly, from the skeleton if and when it is administered properly. This applies especially in the case of infants and small children, whose danger is great because of their excessive body burden and the frequent accessibility of further lead to be absorbed from their environment.

In my view, however, on the basis of a very considerable amount of evidence, the provocative use of the agent for diagnostic purposes is irrational and fraught with error. I have never seen any evidence that inorganic lead is distributed in an erratic manner in the tissues of the human body. In fact, the pattern of the distribution of lead, as we and others have seen it (see the Oak Ridge data of Dr. Tipton and her colleagues), is so consistent that there are no grounds, so far as I know, for the belief that it changes significantly (except, perhaps, in response to chelate therapy). If this is true, the proper method of determining the body burden of lead, is that of establishing the concentration of lead in one or more of the main tissues, and from this calculating the body burden or in appraising its relative magnitude, as compared with the normal lead content of the body. Our experimental work has provided the basis from such calculation or appraisal.

Now, when the chelating agent is administered, an unpredictable response, both in time and in quantity, is found to occur, on the part of the rate of the urinary excretion. We have no real information on which to appraise it, quantitatively, for we do not know, in biochemical terms at the cellular point, in various tissues, just what occurs. Therefore it is possible only to give statement to a rule of thumb for the interpretation of the result, and the interpretation is just as likely to be wrong as to be right. This is,

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indeed, a poor basis for any interpretation of the amount of lead in the soft tissues as a whole, and for deciding what, if any hazard, is entailed therein. As a diagnostic procedure this is empiricism at its worst, for it is empiricism based on a false physiological premise. By all odds, the best way to find out the general order of magnitude of the body burden, and its significance (on the purely pragmatic basis of what can be observed to be the ^{likely clinical} consequences of too great a body burden), is to see to it that the metabolism of lead in the body is not disturbed by any known therapeutic agent, and then to measure precisely (and repeatedly if necessary) the lead content of the blood. (That of the urine has too much physiological variability to be depended upon.) If the latter is high, intermediate or low when the blood is in equilibrium with the other tissues (i. e. undisturbed metabolism), the body burden is, in general correspondence, high, intermediate or low. This is sound physiology, so far as anyone now knows. If there are exceptions, they have not come to light nor been interpreted. I do not hold that there are not exceptions, but I have never seen them, and I have certainly looked longer and more carefully than has anyone who has written on the subject. I know that my view of this matter is not shared by all of the clinicians, including, vociferously, some of our French colleagues. However, they have not provided evidence, but only vigorously expressed opinions. I have no hesitation in expressing myself to you with somewhat corresponding vigor. This has come to be a fairly important matter in compensation medicine, in which I have been involved not infrequently. This feature of the matter is troublesome, of course, but of much more importance is this issue as it relates to a person who seeks medical care and advice. It is most disturbing to a man who has been exposed to lead without illness or after recovery from illness, to be led to suspect that the ultimate effects of his exposure are unpredictable, and that he has the potentialities of sequestering potentially dangerous quantities of lead in certain of his soft tissues. There is not the slightest evidence now that this is true, and I hope that we shall not contribute to this kind of apprehension, unless, indeed, we should find it necessary, in clinical experience, to guard against undue optimism, concerning the outcome of unusual cases of ptumbism.

With kind regards,

Sincerely,

Robert A. Kehoe, M.D.

RAK ef

cc: R. T. Johnstone, M.D. (blind)