

June 18, 1958

Dr. T. George Bidder
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Dear Doctor Bidder:

I cannot call to mind all of the data obtained in animal experiments, but, off-hand, I do not remember any that would answer your purposes. I think I can assure you that you will not be able to find any satisfactory evidence of a precise correlation between the concentration of lead in the blood of men and that in their brain, except under certain very limited conditions. This does not mean that there is no such a relationship but that it is an inconstant one, dependent upon the time factor. It is also necessary in speaking of such a relationship to confine one's remarks to inorganic compounds of lead. When tetraethyl lead is absorbed, for example, the lead content of the brain may become very high without any appreciable or measurable elevation of the blood lead.

If there were sufficient data in a sufficient variety of situations, some such relationship would be found. In order to explain my meaning, I must describe the metabolism of lead in the animal or human body, as it has been pieced together into a fairly comprehensive pattern through observations made at different times and under a variety of experimental and clinical conditions. Under ordinary circumstances lead is absorbed in normal quantities daily. Under these conditions there is a pattern of distribution of lead in the body whereby a relatively high concentration is found in the skeleton and much lower concentrations are found in the soft tissues, including the brain. The blood is relatively high in lead, as compared with certain other metallic elements that pass into and through the body regularly, because it combines with something (probably a complex organic phosphate) in the erythrocytes, the mean normal concentration being about 0.026 mg. per 100 grams of fresh whole blood. The mean normal concentration in human liver, kidney, spleen, muscle and brain are 0.13, 0.027, 0.030, 0.010 and 0.013 mg. per 100 grams of fresh tissue, respectively.

Whenever there is a significant and maintained increase in the absorption of lead - as, for example, under conditions of occupational exposure, or more particularly when the individual or group ingests lead regularly at a higher than normal level, there is a progressive increase in the lead content of the tissues of the body generally. The greatest increase in concentration is in the skeleton, but the soft tissues, including the blood, share in the increase.

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There is some question about the behavior of the brain in this regard, and it is believed by many people, without suitable evidence, that there is a barrier which prevents absorption into the brain unless the concentration in the blood exceeds a certain undetermined level. This view may be doubted because of the fact that the brain contains lead normally. It would appear that there is some equilibrium between brain (and other organs) and the circulating medium, whereby under any set of conditions there is a pattern of distribution. Thus in fatal lead intoxication in children (which has provided most of the valid data on human beings) we find relationships of which the following are typical:

Distribution of lead in fresh tissues in mg. per 100 grams (Children)

Liver	Kidney	Brain	Flat Bone
		0.35	13.0
3.27	0.61	0.29	10.65
4.00	0.88	0.58	26.80
3.91	- - -	0.24	17.00
4.40	2.59	0.42	17.90
2.96	1.74	0.50	- - -

These cases have the advantage, from the aspect of lead metabolism, that the duration of exposure to lead has been relatively brief and fairly continuous, as compared with adult cases in which the exposure is likely to have been both prolonged and intermittent. The time factor can disturb the relationships greatly for a number of reasons.

It is difficult to be sure of the concentrations of lead in the blood at the time of death. I know it is greatly elevated in all of these instances, but actual data were not always available in our early case material, and the later findings are complicated somewhat by the therapeutic measures that have been taken. I feel reasonably sure that I have satisfactory data in the files, but I have not had time lately to put them together and study them. In the group of cases above, without taking time to go back to the records, the concentrations in the blood probably ranged from 0.16 or 0.20 mg. per 100 grams to values as high as 0.40 or perhaps even 0.60 mg. per 100 grams. This is sufficient to show the trend of events, and I doubt very much if anything better than this gross relationship can be established.

Data on adult tissues, generally speaking, in relation to inorganic lead, are not available and are not likely to be, for the reason that fatal lead poisoning is a rare occurrence in the adult, and for the additional reason that necropsy material from persons who have worked at a lead trade until death (from a variety of causes) has overtaken them, is hard to obtain. I have been on the look-out for such material for years with but little success (for the reason I gave before, my case material related to tetraethyl lead is not applicable to the problem of inorganic lead).

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I trust that the information which I have given you will be of some interest to you.

Cordially yours,

Robert A. Kehoe, M.D.

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P.S. I take satisfaction in your remarks about the article on Lead in Tice's system of medicine despite the fact that my contribution to it was (so far as the writing is concerned) very small. I induced Jim Hughes to prepare the article and I made only a few suggestions. It has my approval, of course, but the work was his.

R.A.K.

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