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IN REPLY REFER TO:

January 10, 1966

Dr. Robert A. Kehoe
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Dear Dr. Kehoe:

I am indebted to you for your letter of December 23 for it makes me take a more critical look at the questions which you raise. I do believe that chronic or recurrent acute infections may have a deleterious effect in the growing child upon the ultimate outcome of chronic lead intoxication, particularly if there are repeated or chronic infections during the first year following the child's recovery from acute lead encephalopathy and his removal from abnormal lead exposure. The data which I personally have to support this are scanty. They are mentioned in my paper entitled "Quantitative Urinary Coproporphyrin Excretion and its Relation to Edathamil Calcium Disodium Administration in Children with Acute Lead Intoxication" a reprint of which I am enclosing. The pertinent paragraph is found on page 1134 and 1135 which I have marked. I have looked up the data upon which the statements in this paragraph are based and can give you some more detail.

The evidence is based upon studies in five children during acute bacterial infections (pneumoccocal pneumonia-2, streptococcal tonsilitis-3) which occurred two to twelve months following recovery from acute lead encephalopathy. All had been removed from abnormal lead exposure. Serial blood lead determinations showed continuous decrease in blood lead concentration and no rise at the time of the acute infection. Two of the three patients who showed a significant increase in urinary coproporphyrin excretion received EDTA as well as treatment for their infection. In response to EDTA administration, their urinary lead excretion increased to quantities comparable to the outputs shown in figure 2 of the enclosed reprint. In other words, they responded just as well as those children without acute intercurrent infection. Two of these patients had a number of other studies. The only abnormality found was an increase in cerebrospinal fluid protein content at the time the urinary coporporphyrin was elevated. One of the two patients who had acute bacterial infection and showed no rise in urinary coproporphyrin output also showed no significant increase in urine lead excretion when EDTA was administered. Subsequent random observations in growing children have shown that the urinary coproporphyrin falls when the infection is brought under control with appropriate antibiotics. If one waits until the urinary coproporphyrin decreases and gives EDTA at that point

there will be no significant increase in urine lead excretion. Granted, these represent observations on a very few patients, but I believe they are valid and I might say we use them in the clinic now in the sense that any child recovering from lead intoxication who has acute infection always get a urinary coproporphyrin determination and receives treatment if the output is significantly increased.

I have concluded from these data that acute infections, particularly during the early recovery phase, can cause an increase in the "chelatable" lead. The source of this lead is, of course, a matter of speculation. It may simply be that there is a redistribution of lead within individual soft tissue cells in the presence of infection and that the lead is merely removed to another compartment within the cell or bound to a different protein where it is more accessible to EDTA. My assumption that some of the lead which is excreted may come from bone is certainly based upon indirect information, but it should be noted that growth arrest lines regularly occur with each infection in the young growing child. The lines seen by x-ray represent the fact that new bone is not being laid down in the presence of infection. This, in turn, may interfere with the normal deposition and redeposition of lead on the bone crystal. At this time, it seems likely that such lead might be released into the circulation and taken up by the soft tissues; however, I have no direct evidence on this point.

I originally became interested in the relationship between infection and chronic lead intoxication because of the observation in a few patients that the permanent brain damage suffered by them seemed out of proportion to both the length of the initial abnormal lead ingestion and the severity of the initial acute illness. I noted in their records that they suffered repeated acute respiratory infections during the first year following their removal from abnormal lead ingestion. I have also seen four children who have demonstrated peripheral neuropathy of the type reported in chronic lead intoxication. The neuropathy in these children occurred in association with infections during the winter following their recovery from acute lead encephalopathy. At the times these episodes of neuropathy occurred, we could find no evidence of renewed abnormal lead ingestion.

Thus, I do believe that repeated infections during the first six to twelve months following removal from abnormal lead sources can have a deleterious effect in terms of causing an exacerbation of lead intoxication. Repeated minor insults may be cumulative and thus worsen the ultimate outcome. I would agree with you, however, that this problem should be more carefully worked out. I hope during the coming year to begin a study on the chronic phase of lead intoxication in children and this is certainly one of the points on which we shall try to obtain better data.

I hope I have answered the questions in your letter of December 23 clearly. If not, I do hope you will write me. Again, many thanks for your letter.

Sincerely yours,

J. Julian Chisolm, Jr., M.D.
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JJC:jb