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Dr. R.A. Kehoe,
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OUR REF.

YOUR REF.

24th February, 1970.

Dear Dr. Kehoe,

I returned from Puerto Rico last Friday, February 20th, after what turned out to be an interesting, though from the point of view of the public health, a somewhat disappointing meeting.

The poisonous effects of lead on the kidney, haem synthesis, enzyme activity and the central nervous system were considered at great length, but at lead concentrations which were extremely high relative to anything that one might consider to be normal, or even unusual, exposure in man.

Dr. Goyer spoke of renal tubular disease, the appearance of inclusion bodies, and the development of renal adenomata, in rats fed on a diet containing 1% lead acetate for continuous periods in excess of a year. He had little information on rats in which the diet contained less lead, but did indicate that at a concentration of lead acetate in the diet equivalent to 400 parts per million, no effect was noted in kidney tissue, except when the rats were, in addition, provided a diet which was low in calcium content. Under these circumstances an increase in ALA in urine was noted down to about 200 ppm lead acetate in the diet.

Professor Goldberg, from the Department of Medicine at the University of Glasgow, discussed the importance of the interference of lead with ALA dehydrase. He indicated that at a concentration of lead in the blood of 20 micrograms per 100 grams it was possible to detect a reduction in the ALA dehydrase in serum. He intimated that children are particularly sensitive to the effect of lead on ALA dehydrase. There was a good deal of argument as to whether this effect of lead was of any significance, or if it occurred at all in vivo, since these investigations had been undertaken in vitro.

Dr. Shreiner talked of nephro-sclerosis as being caused by a multiplicity of agents, including lead. He described, also, two cases of tetraethyl lead poisoning in leaded gasoline tank cleaners, in which both showed evidence of porphyria. Biopsy of kidney tissue in these two cases showed evidence of tubular damage.

Dr. Bricker spoke of the physiological activity of lead in the kidney, and Dr. Morgan described the appearance of gout in a number of negroes from Alabama, who had been drinking "moonshine" for a number of years. She agreed it was not possible to say whether the effects on these men were due to the alcohol, or to

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the lead, but considered that probably lead was the main cause of the disease, since, in some of these alcohols, 400 milligrams of lead per litre was detected. There was a great deal of discussion on the effects of haem synthesis by Drs. Chrisholm, Jensen, Cramer, Griggs and Goldberg. However, it was agreed by practically all the investigators that they had used very high levels of lead in the diet (up to 5% lead acetate) to provide the effects that were noted in rats.

Dr. Feldman discussed neuropathological changes resulting from lead absorption in children, and indicated that neuropathy had been reported in children with levels of lead in the blood of less than 40 micrograms per 100 grams, reporting one case in which the level of lead in the blood was only 13 micrograms per 100 grams. He indicated that in all these cases the level of coproporphyrin in the urine was increased. He indicated also that long periods of exposure to tetraethyl lead caused brain changes, and quoted the work of Vardanis and Quastel. A number of us were very sceptical of some of Dr. Feldman's statements and also of the low levels of lead in the blood of children, that he quoted.

Jim Stopps, from Dupont, gave a brief survey of the work that the Haskell Laboratories were undertaking with respect to effects of lead at varying levels of concentration in the diet in animals, i.e. in rats and dogs, and indicated that no effect was noted at concentrations of lead in the diet of less than 400 parts per million. He described, briefly, the population studies that DuPont, together with other organisations, are at present undertaking, or proposing to undertake. These include the Wenatchee, Washington State, apple orchard community, the study of a community near to a lead smelter in Yugoslavia, the TEL workers at DuPont, a follow-up of Professor Lane's work (which is being undertaken by Dr. Malcolm at Manchester) and the work that the ILZRO are proposing to undertake on lead workers in various parts of the world.

Dr. Roush gave a review of the level of lead in the environment, as this relates at the present time to soils, water, air, food and the lead in the human body, as represented in urine, blood, and bone tissue.

I made some reference to our autopsy studies, indicating that in the soft tissues that we had examined, concentrations of lead remain remarkably stable throughout life, although we have not found this to be so in bone. I made some reference later to lead concentrations in hair, as this was mentioned by Dr. Feldman, who had suggested that the hair could be used for screening purposes in cases of suspected lead exposure. I indicated that our findings, both with respect to non-occupational and occupational exposure to lead, gave only a rough indication of how much lead a person may have absorbed, particularly as we cannot say for sure that the lead in hair represents the lead concentrations in the body, since it is quite possible that lead in the air external to the body may have become incorporated into the hair through the sulphydryl groups. Dr. Chrisholm agreed that this was possible.

At one stage during the proceedings (on the second day) the Chairman of the meeting, Dr. Carl Moore, indicated that, had he been invited to the meeting as an authority who required to be convinced of the ill-effects, or otherwise, of lead on human beings, he would, up to that stage, have been as unconvinced as he was at the beginning of the meeting. He indicated that his impression was that our methods of detection of concentrations of lead and the effects of these on the human system were too crude to provide us with an accurate estimation of that level of lead which would not produce an effect, and thus be considered to be acceptable.

Dr. Vallee spoke at some length on the effects of lead on various enzyme systems and suggested that, although there is no evidence at the present time to show that lead has a necessary function to perform in the normal activity of body systems, he believed it was quite probable in the course of time that this would be shown to be so, as had happened in the past with some of the other metals, such as copper, manganese and cobalt. He did not press this idea too far, but did stress that because high concentrations of lead are poisonous, it does not follow that low concentrations are a little poisonous (an aspect to which you yourself have often made reference).

I have no doubt that you will receive a full report on this conference from Lloyd Tepper and others who were there, but I send you these comments for what they are worth. There was a feeling at this meeting, of a somewhat positive nature, that lead in gasoline, irrespective of the outcome of meetings such as was held in Puerto Rico, is to be eliminated altogether or drastically reduced in the United States within a relatively short space of time. I do not know how true this is, but certainly I came away far from reassured as to the future.

Thank you very much for returning to me our manuscript on the concentrations of lead in human tissues and for the time that you devoted towards editing and correcting it in detail. As I mentioned to you previously, I had already sent the paper to the Editor of the British Journal of Industrial Medicine, before your comments came to hand. I have not yet heard from him, but as I am sure he will require me to make changes in the manuscript, I will have an opportunity to incorporate most of your suggestions in the finished paper.

I hope all is well with you and Lucille. The flyrod has not yet reached us, but as soon as it appears I will certainly let you know.

With kindest regards,

Yours sincerely,

Pat Bang