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Department of Occupational Health
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Professor R.S.F. Schilling.

January 7th 1966.

Professor R. A. Kehoe
College of Medicine,
University of Cincinnati,
Eden Avenue,
Cincinnati, Ohio.

Dear Professor Kehoe,

Thank you so much for your very detailed and helpful letter; and for the reprints.

I was glad to hear you are continuing experiments with lead inhalation. I am particularly interested in its estimation using personal samplers and would like to prove mathematically that blood lead, say, is the best index of exposure, but not necessarily of poisoning; whereas ALA say might be the best index of tendency to poisoning - but not of exposure. For example, some cases of clinical lead poisoning have blood leads of 110 ugm/100 ml: whereas some workmen without poisoning have 400 ugm/100 ml. (a 300% increase). It would be nice to show that no-one with ALA less than x units has clinical poisoning, but everyone with x + 50% has clinical poisoning.

I wonder if workers in this field on the whole do not distinguish sufficiently between the use of certain biological indices to estimate exposure, and the use of the same indices to estimate the tendency to poisoning. I wonder if you agree?

I certainly agree with your point (page 2) that lead poisoning is diagnosed clinically and not by analytical means. That is why I am less happy when you say (page 3) that a reduction in haemoglobin due to lead is lead poisoning. For the reduction may only be detectable by analytical means, and not clinically - so I would prefer to call the case "excessive lead absorption" (and grossly excessive to be sure!)

Admittedly, men with lowered haemoglobins, but no symptoms and denying "tiredness", when removed from lead say later that they feel much better, and were tired before. But one would call this poisoning from the symptoms rather than from lowered haemoglobin.

Similarly, I am not happy to call unusual quantities of coproporphyrin in the urine (analytical test), lead poisoning, in the absence of clinical symptoms and signs. A very little lead causes an increase in porphyrinuria - where then can one draw the line and say this is an "unusual quantity" and therefore = lead poisoning? Increased porphyrin in urine is certainly a sign of interference with a physiological process, and an abnormal metabolite appears in the urine. But an abnormal metabolite appears in the urine after drinking a pint of beer - yet again we do not say this is a sign of alcoholic poisoning.

I was very interested to hear your hypothesis that poisoning may be precipitated by the release of lead from cells. I too had imagined that possibly when the red cell becomes "poisoned", it may release some of the large amount of protein bound lead it holds; which in turn, as ionic lead, increases the plasma ionic lead concentration which initiates further stages of poisoning - a sort of trigger mechanism which could be fired earlier by illness, alcohol, dietary deficiency and other factors noted in the past. This incidentally might cause a lowering of the total blood lead, accounting for poisoning with "low blood lead" and non-poisoning with high - I would like to do some animal experiments on that.

I take your point about not adding to unproven hypotheses in the literature, and agree that normally this is a very undesirable approach. But I feel strongly that a lowered red cell volume must reduce the "lead-carrying power" of blood, and therefore there are good grounds for deducing a correction factor for "observed total blood lead" to get the "corrected blood lead" in cases of lowered haemoglobin. So I am publishing the suggestion in a subsidiary paragraph of a paper in Brit. Journ. Industr. Med. next April, very tentatively to stimulate thinking on this line - I hope this meets with your approval. The paper, incidentally, is on blood lead and haemoglobin and demonstrates (yet again!) that haemoglobin is not a good control - though better than nothing, which is why the legislation was introduced in this country.

Again, very many thanks for your letter and reprints. I hope this letter isn't too long - it would be a great privilege to talk sometime instead! I hope that may be possible someday.

Yours sincerely,

M. K. Williams.