

A.S.A. Z-37, COMMITTEE ON NEW SUBSTANCES

Manfred Bowditch to J.J. Bloomfield, June 8, 1948

Lead is certainly not a "new substance" and it may well be that my thoughts on this subject are not appropriate for your special committee's consideration. I think, however, that a start should be made towards substituting separate standards on some of the more common and toxicologically widely differing lead compounds for the present blanket standard of 1.5 mgm. per 10 cubic meters. You may perhaps wish to discuss this with Lawrence Fairhall and let me know how you think the subject might best be broached to the full committee.

Another item in which I am interested is the possibility of setting up some sort of standards for stippled cell counting methods. I have discussed this casually with Bill Machle, but nothing more. Is this in your opinion a suitable subject for the Z-37 committee's consideration?

COMMENTS ON THE ABOVE

A. G. Cranch

Yours of June 11 received with excerpts from your letter of June 8 to J.J. Bloomfield. Am heartily in accord with the ideas you express in that letter. Certainly I think there is enough difference in hazard in various forms in which lead is used industrially so that it would be very well to consider the advisability of separate standards for some of the more commonly used forms. Would be glad to see such a discussion brought up at the ASA Z-37 meeting.

The second point you bring up is also quite pertinent as I have noted that in different locations the doctors use quite different standards in the interpretation of stippled cell counts to say nothing of variations in technique. Whether this particular point is one which is a suitable subject for discussion by Z-37 I am not prepared to say. It seems to me that the scope of this committee might be too limited to bring in a discussion of a standard for diagnosis based on blood examination. It is concerned more with the limits of contaminants in the atmosphere and methods of their determination than with diagnostic procedures. Perhaps this subject can be better approached through some other agency.

Philip Drinker

Thank you for the two paragraphs from your recent note to Bloomfield. We have a study on now at St. Joseph Lead's plant at Bonne Terre which will, I hope, show what the St. Joseph Lead men and I believe very strongly and that is that the toxicity of lead sulphide as galena is inconsequential compared with that when galena is roasted. I am sure Felix Wormser feels just as strongly as I do on this point. Therefore, I think your suggestion is timely.

L. T. Fairhall

Jack Bloomfield and I have discussed the matter of variation in toxicity of the different lead compounds and the present blanket standard for lead of 1.5 milligram per ten cubic meters of air.

You may recall that Jack and his associates set up this standard originally (PHS Bull. No. 205) and it was based upon exposure to the oxides of lead and lead fume. Since then it has been widely, if not universally, accepted as a basic standard of lead. I realize that the toxicity of lead compounds varies tremendously from lead tetraethyl to galena. Lead compounds such as lead phosphate, galena and lead silicate, or lead frit are now recognized as far more insoluble in tissue fluid and therefore more inert than the lead oxides and carbonate or even the sulphate (PHS Bull. No. 253). However, Kehoe does not consider that there is this variation in lead compounds. Even with such a toxic substance as lead tetraethyl he states (Tetraethyl Lead Poisoning. J.A.M.A. 85: 108, 1925) that "Nevertheless, it cannot be doubted that the lead is the essential toxic agent in the compound (lead tetraethyl). In fact, its toxicity is of the same order of magnitude as that of other well known compounds of lead." (*Italics mine.*) He also states (J. Lab. Clin. Med. 6: 554, 1927) "On the toxicity of tetraethyl lead and inorganic lead salts, its (lead tetraethyl) toxicity varies little from that of other and water soluble lead compounds. This fact indicates that its toxicity is a function of the lead and not of any peculiar qualities characteristic of the compound."

I quote these extraordinary opinions because you may find some opposition to the fact that lead compounds do vary in toxicity. However, and quite apart from the above, I feel that to use different MACs for lead or its compounds would lead to much confusion. I have never felt that there was any disagreement by the Lead Industries Association with the basic MAC value for lead. Where galena or lead frit are involved I would a) either exempt these from a MAC value altogether, or b) leave the matter to the common sense of the industrial hygienist.

With regard to the standards for stippled cell counting methods, I would suggest you get in touch with Elston Belknap of Milwaukee, Wisconsin, who has done outstanding work in this field for twenty years or more.

W. J. McConnell

In reply to the extract of your letter to Jack Bloomfield regarding separate standards for widely differing lead compounds, I fully appreciate your feelings with respect to the inconsistency of using a blanket standard for lead compounds of varying toxicities.

On the other hand, there are so many physiological factors which may cause variations in human toxic thresholds, not to mention factors which may cause variations in environmental concentrations of the materials, that I question whether we should place too much dependence on the security offered by so-called safe standards. It seems to me that such standards can only be very roughly approximated. Therefore, the present standard which has been accepted might well suffice for all compounds of lead. I doubt whether more precise standards could be approximated.

W. J. McConnell (Continued)

With respect to standards for stippled cell counting methods, I believe Dr. Hamilton has suggested certain standards. Here again, I don't think that laboratory tests can be substituted for intelligent observation and evaluation of the worker as an individual by an informed physician. I don't think that blood examinations should be confined to stippling alone, but a red and white cell count, a notation of changes in color or morphology of the red cells, and any drop in hemoglobin should be included. Variations from normal lead content in the urine should also be made. These laboratory data, together with the clinical symptoms and signs, must all be evaluated in arriving at a diagnosis and I would hesitate to emphasize any group in particular.

C. P. McCord, June 16

In your letter of June 11 you ask me to comment on an excerpt of a letter to Mr. Bloomfield.

For a long while some of us have firmly felt that by no means are all lead compounds equally dangerous due to distinct differences in solubility rates. This was long discussed at an earlier time in ASA meetings. It was then agreed that substantial differences as to prospects of lead poisoning from different compounds existed but to the majority it seemed inexpedient to make any demarcations. It appears practical that the long list of ordinary lead compounds might be broken down into three zones, with the first conforming to the present standard of 1.5 mg., a second possibly leading to a 3 mg. level and the third, remotely possibly reaching as high as 6 mg. I realize that this last figure may be anathema to some, but the warrant may still exist for a few compounds. By no means do I commit myself to any such figures.

Long ago William Fredrick and I set up a number of lead zones somewhat in line with the above statements. I am suggesting that you write him for a copy of our listing. Bill is so given to stringent standards that any statement from him toward liberalization to the present situation would be almost the last word in needed changes.

As to your second point, that is standards for stippling, I am less enthusiastic. Stipple cells in the blood in lead poisoning or otherwise, partly may be regarded as accidents. By no means do they represent the total number of red cells containing basophilic material. The number of stipple cells formed in lead poisoning in my opinion is a frail index of the severity of lead poisoning or the imminence of its appearance. The artificial clumping of all basophilic material in red cells (basophilic aggregation test) is much superior but still should be regarded chiefly as a screening procedure. Regularly we make use of this procedure in group examinations of suspects and with highly helpful results. We would never rely upon this as a final criterion in diagnoses. It is my thought that you should neither press the item of stipple cell standardization nor place too much emphasis on its conclusive value in diagnoses. No less, positive results are quite helpful along with several other items such as quantitative lead determinations in urine, in an overall appraisal of the diagnostic situation.

C. P. McCord, June 24

There are two small objections to your including my recent letter in your compilation on tolerable lead exposure levels.

The first of these is that I do not want to appear to be working behind the back of the Z-37 committee.

The second is that the very high figure that I mentioned for a few lead compounds may not be regarded as an exact one and is not based on actual experience. While I do believe that the standards should not be uniform for all lead compounds and should be liberalized for many, I do not want to be credited as sponsoring any exact high figure at this time. If this present letter be included along with the earlier one for discussion purposes, I will have no objection to the use of both.

H. H. Schrenk

With reference to your question regarding the permissible limit of lead, I appreciate very definitely problems involved. There are a large variety of lead compounds and the permissible limits for individual ones could vary widely. It seems to me that this question might well be placed before Committee Z37 again as well as before the G.I.H. Committee. The question of stippled cells might also be placed before Z37 because I believe that most of the people who have worked with this procedure are members of the committee and therefore the committee would be in a position to discuss the subject intelligently.

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June 30, 1948

Mr. Bloomfield
Dr. Cranch
Prof. Drinker
Dr. McConnell
Dr. McCord
Dr. Schrenk

A.S.A. Z-37, Committee on New Substances

Referring to our recent correspondence, herewith are the quite varied comments of the several members of our committee (J.J.B. says "When you heard from Lawrence Fairhall, you heard from me also.") on the suggestions in my letter of June 8 to Mr. Bloomfield.

While I have always believed and said (cf. Jour. I. H. & T., June 1940), as does Dr. McConnell, that we should not "place too much dependence on the security offered by so-called safe standards," I find it difficult to foresee that "to use different MACs for lead or its compounds would lead to much confusion." Could not the same argument be put forward for a single MAC for benzol, toluol and xylol?

Be that as it may, we surely have here the basis for some useful discussion.

Manfred Bowditch



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