

October 11, 1941.

Mr. R. L. Forney, Director,  
Industrial Division,  
National Safety Council,  
20 North Wacker Drive,  
Chicago, Illinois.

Dear Mr. Forney:

I am returning to you herewith the second and third drafts of pamphlet #3, "Lead", which you were so kind as to send me for an examination.

It was quite impossible for me to review the second draft at the time it came to me, but I have taken the time to review the third in some detail and to make numerous suggestions. You will find my comments attached to this letter. I am sending also a carbon copy for your convenience. I trust my comments will be found to be useful, and wherein they appear to be critical, I hope you will recognize that it has been my purpose to be brief and to the point, and yet, I hope, not arbitrary. There has not been time to cover the whole pamphlet, and thus, I have indicated my willingness to follow through with my suggestions if your committee wishes me to do so.

The revisions which I have suggested are based in large part on the content of the report of the committee on lead poisoning of the Industrial Hygiene Section of the A.P.H.A., of which I am chairman. We are preparing a rather comprehensive report, a portion of which is completed and will soon be issued. So far as it is feasible to do so, I have attempted to bring this pamphlet into harmony with that report, with the idea that it would be disadvantageous if the two were to clash with each other. On the other hand, if they are in essential agreement, they will strengthen each other measurably, especially in relation to compensation and other medico-legal considerations.

Other corrections or suggestions have been based on the following purposes; (1) The removal of names so far as possible, except insofar as definite reference to published articles can be cited; (2) The avoidance of controversial statements, particularly when they are unnecessary for practical reasons; (3) the avoidance of discussions of medical matters so far as possible so as not to raise too many medico-legal difficulties; (4) the elimination of relatively unimportant matters for the

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sake of brevity and conciseness; (5) the correction of ungrammatical and ambiguous statements. In many instances the explanation for a given criticism or suggestion has been offered in the paragraphs which I have prepared.

Obviously, I do not expect your committee to accept my corrections verbatim. I do wish, however, to stress the fact that every correction or suggestion which I have made has been based on careful consideration and on a rather broad experience. I should particularly hope that any authorized pamphlet of this type would avoid controversy over certain relatively unimportant matters and that it would not contribute to keeping alive a number of the misconceptions which have been disposed of by recent investigation. I wish to urge particularly careful attention to the question of analytic methods. The pamphlet, as represented in the third draft did not deal with this question realistically. What I have done with this portion may well be subject to improvement, but the general manner of dealing with the problem of methods is in line with the judgment of the people who have had the most experience in this field during the last ten years. I can speak not only for myself and my associates, but also for a number of others whose experience has been broad. Anything that is issued on this matter ought to be up to date and in accordance with recent experience. This matter is quite serious, since a very great proportion of the present confusion as to the significance of analytical data is based on uncertainty and ineptitude in the choice of methods of analysis. Your committee, therefore, should be very cautious in its recommendation of methods and should not authorize the use of any method which is not published in minute detail, and which has not been tested critically by competent workers.

Very truly yours,

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Robert A. Kehoe, M. D.

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Page 1

1. "eliminate---"through tests and analyses of samples"---3rd line  
Change as follows---"processes through properly designed  
operating, ventilating, and exhaust equipment"-----4th line  
Change as follows---"While the avenues of lead absorp-  
tion into the body and the toxic effects therein will  
be covered"-----6th and 7th lines

Page 2

6. Change as follows---"precautions should be taken against  
hazardous lead exposure on the part of employees."---Lines 2 and  
1 from bottom

Page 3

7. Omit reference to slow absorption of lead in oil as prac-  
tically unimportant and change sentence as follows:-  
"Tetraethyl lead is an oily, liquid, organic compound of  
lead that is dangerously volatile at ordinary tempera-  
tures. It is also readily absorbed through the healthy,  
unbroken skin. For these reasons, it is a highly dan-  
gerous material and must be manufactured and handled with  
great care against inhalation of vapor and contact with  
the skin. It is used chiefly as an anti-knock agent in  
motor gasoline to which it is added in low concentrations  
that do not give rise to the danger of lead absorption  
among persons who handle and dispense gasoline. Tetra-  
ethyl lead has also been used in small quantities in the  
manufacture of other chemicals. Regulations governing the  
use of tetraethyl lead.....etc."
8. Change as follows:---"Commercial products containing lead  
compounds are not always described or labeled in such a  
manner that the managers, foremen, or workmen in an indus-  
trial plant or process are aware that they are using lead  
compounds. When such commercial preparations are supplied  
for use, it should be the practice of the supplier to point  
out the potential lead hazard associated with the use of  
the product by employing suitable warning labels. Employees  
may.....etc."
10. No useful purpose is served by emphasizing the factor of  
individual susceptibility. To do so encourages men to be-  
lieve that they can ward off effects that would injure  
weaker persons. Moreover, there is much less validity in  
the idea of special susceptibility than is commonly be-  
lieved. Still further the question of dosage is so great-  
ly modified by the time factor that the acute toxic dose  
is of little consequence in relation to occupational lead  
exposure. The whole question of immediate toxicity should  
be soft-pedaled, therefore, while stressing the importance  
of avoiding unknown and uncontrolled exposure to all lead  
compounds.

It is also important to avoid the discussion of the uncom-  
mon effects of lead intoxication and to call the attention  
of laymen to the more usual and characteristic effects, so  
that they may avoid undue apprehension on the one hand and

may recognize the existence of danger on the other.

I should revamp this paragraph as follows:

"Whenever there is lead exposure there is potential danger from the absorption of lead. The degree of danger depends upon the extent and duration of the exposure. The poisonous effects of lead absorption are usually manifested in one or more of the following ways:

- (1) By disturbances of the digestive system, in the form of loss of appetite, constipation, vague abdominal discomfort, and in more severe cases by severe cramping abdominal pain (colic);
- (2) By painful and stiff joints, bones, and muscles;
- (3) By general weakness, loss of weight, and pallor;
- (4) By loss of strength in the fingers, hands, or forearms, and inability to use them in the performance of customary tasks;
- (5) By damage to the blood with the production of anemia."

(Note that no reference is made here to "stippling" or "lead line". This omission is deliberate and necessary, because these are not "poisonous effects".)

Too much stress has been put on kidney damage and injury to the reproductive system in connection with lead poisoning. These are definitely controversial matters from a medical point of view and should not be presented thus factually without adequate discussion. It is better here to omit reference to them by calling attention to the more common effects.

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11 and 12. I should omit these sections altogether. They give little or no useful information to industrial executives, hygienists, or physicians, and they confuse the issue, which is covered better in paragraph 13. Paragraphs 11 and 12 are technically erudite, but practically unimportant except to the toxicologist. This pamphlet is directed at the specific problem of prolonged occupational lead exposure. The issue should be stated clearly by emphasizing certain statements in Paragraph 13 as follows:

13. It must be recognized that virtually all compounds of lead are poisonous if they are handled in such a manner as to be introduced regularly or frequently, in sufficient quantity, into the air breathed by industrial workmen, or if they are taken into the mouth and swallowed in sufficient amount over a long enough period of time. Some compounds

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of lead are more dangerous than others for a variety of reasons. Some are more soluble in the tissues and fluids of the body than are others. Some of them must be employed or processed in a physical state that makes them difficult to handle without danger of exposure. Thus it may be feasible in some instances to select a relatively safe lead compound for a specific industrial purpose in place of one that would give rise to a much greater potential hazard. Nevertheless it should not be believed that preventive measures can be neglected or reduced in effectiveness, because the compound or compounds in use are allegedly low in toxicity.

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14. Change as follows:---"Lead and its compounds can be taken into the body by inhalation or by ingestion (swallowing). (Tetraethyl lead is readily absorbed through the skin. See paragraph 7.) Inhalation of lead is by far the most common and most dangerous form of industrial lead exposure. It should not be assumed, however, that it is unnecessary to warn and protect industrial workers against the ingestion of lead compounds, and against careless and unnecessary skin contact with lead compounds. Every effort should be made to encourage and facilitate the development of care and cleanliness on the part of workmen, not only to avoid lead absorption, but also to avoid dermatoses."

(I should require excellent evidence before I could accept the statement that lead in oil is absorbed in appreciable quantities through the healthy or injured skin. Is there such evidence, either clinical or experimental? Unless there is uncontrovertable evidence, this reference to it should be deleted entirely.)

15. Change as follows:---"The remainder is deposited on the surface of the lung tissue from which it is absorbed and distributed into the tissues of the body." (It is unnecessary and unwise to describe questionable physiological mechanisms. It is quite improbable that lead is carried in the blood as the phosphate, and there is no point here in making a statement that most investigators will criticize. In point of fact practically all the lead in the blood is carried in the red blood corpuscles and no one has the vaguest idea as to whether it is there in organic or inorganic combination.)
16. Change as follows, and for similar reasons:---"eliminated 3rd line through the feces. The greater portion of the lead which is absorbed from the gastro-enteric tract is carried to the liver. It eventually finds its way into other tissues of the body and also back into the intestine by way of the bile."

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17. Delete completely as repetitious and lacking in useful information. Tetraethyl lead is dangerous, not because it is absorbed directly into the blood stream, thereby short-circuiting the liver, but because it goes quickly to the organs of high fat content, that is, the brain as well as the liver. It does not cause an immediate, but rather a delayed intoxication.

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Pages 8

and 9.

25.

Revise as follows: Methods of Lead Analysis

"There are a number of general methods which can be employed in the analysis of lead dusts. Some of these are equally satisfactory for the analysis of lead in biological materials after suitable preparation of such samples. Therefore, it seems advisable at this point to combine all descriptive references to analytical methods and their applications, so far as they can be dealt with in this pamphlet. Only quantitative methods are mentioned, since the mere detection of lead in samples is without value.

26. Methods based on orthodox chemical procedures whereby lead is separated from other metals as the sulphide, sulphate, or chromate, and determined finally by titrametric, colorimetric, or turbidimetric techniques have been described in numerous modifications by various investigators. These are laborious and time-consuming, and are fraught with numerous technical difficulties, but they yield satisfactory results in the hands of careful analysts, if the quantities of lead dealt with are sufficient in quantity, i.e. 0.2 milligrams or more. References to articles describing these methods will be furnished on request, but since these methods have been largely displaced in recent years by more sensitive, more accurate, and more convenient methods, they will not be discussed further.

(References given out here should include not only Fairhall's method, but certain modifications and improvements in it that have been described much more precisely than Fairhall's. They should also include other methods based on chemical separatory principles, a number of which have proved their worth in the hands of Australian, British, and American investigators. Fairly complete reference to these can be found in a number of papers on methods. I shall be glad to supply them on request.)

27. Several electrolytic techniques for the determination of lead have been described and employed with reasonable success by various investigators. These, too, except for certain limited applications have been superseded to a large extent by methods developed more recently.
28. Various modifications of the Fischer-Leopoldi method, (making use of dithizone (diphenylthio carbazone) as a means of extracting lead quantitatively from its aqueous solutions to form a colored complex), have been developed in recent years and have come to occupy first place among procedures for the determination of lead. The method is sufficiently sensitive to deal with the minute quantities of lead present in small samples of urine, blood, and tissues, and when properly carried out, it is specific for lead and quantitatively precise. Several of the modifications have been described in step-by-step detail and can be relied upon implicitly when employed by careful and experienced analysts. Among those used extensively with

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a variety of materials are the methods described by Clifford and Wichmann, by Wilkins, Willoughby, and Kraemer, and by Hubbard.

29. Spectrographic analysis of materials containing lead can be carried out with extreme sensitivity and with accuracy equivalent to that of the best dithizone methods. The method requires highly specialized and costly equipment, and therefore, it is not widely used. Because of this limitation, further discussion of it will not be undertaken here. Reference can be made to the papers of Cholak, et al for details of the technique.
30. Here use paragraph 28 with modifications beginning with line 3 as follows: "It has in its favor the use of comparatively simple technique and somewhat greater speed in the final determination of lead. With this as with other methods, however, the preparation of samples requires time and care, and thereby, a considerable limitation of the speed of analysis is imposed. When properly handled, the method will yield results comparable in accuracy with the dithizone and spectrographic methods." Refer here to the paper of Bambach.

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30.

Maximum permissible concentration (This will become 31 if previous recommendations are followed.) Correct first sentence to avoid repetition of "permissible" and "permitted"; "The lead concentration in workrooms should not be permitted to exceed---"etc.

#### Signs of Lead Poisoning

Pages 10, 11,  
and 12

This section of the pamphlet should be revised drastically, in my opinion, not so much because it is incorrect in its facts, as because it is not directed either to laymen or physicians in such a way as to provide clearly the information required. The layman will not understand the simple facts which he should have, because they are mixed in with strictly medical and physiological considerations. The physician will not accept the medical information because it is not presented in the manner to which he is accustomed. The discussion, therefore, while fairly clear to the specialist, is both too much and too little to accomplish its purpose. In my opinion the discussion of normal lead absorption and the evidences of increased lead absorption should be included in the previous section on "The Action of Lead and Lead Compounds on the Body", since this information concerns lead absorption and could well follow the paragraphs on the "Entrance of lead into the body", just before "Testing for Presence of Lead in Air and Analysis of sample". Such an arrangement would permit the inclusion of a later section for the information of physicians, on "Clinical types of lead poisoning and

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the diagnosis of lead poisoning", this to be substituted for the section now entitled "Signs of Lead Poisoning". Such a section, prepared by a physician for physicians, could be a brief but adequate statement of the present status of the subject, with a few well chosen references to the literature, instead of the partial quotation of authorities. I should be glad to assist in the preparation of such a section in any way possible, but I cannot develop my suggestions in time to meet the dead-line set up in the letter accompanying the draft. I shall also be glad to submit this section of the report of the Committee on Lead Poisoning of the A.P.H.A. as soon as it has been completed, for such use as it may be here. On the other hand, if it is necessary to issue this pamphlet quite soon, I should suggest eliminating this section, merely adding suitable information to the layman to the section on "The Action of Lead and Lead Compounds on the Body".

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While I have not had time to review the remaining material in minute detail, it seems to me to be very satisfactory, except for the last page, on which the lead findings in the urine are expressed in non-quantitative terms. I am sure Dr. Kronenberg would wish to modify this to include quantitative limits in the case of the urine. Reference might also be made to the quantitative analytical findings in the blood.