

EMERY R. HAYHURST, M.D., PH.D.
CONSULTING INDUSTRIAL HYGIENIST
1925 CONCORD ROAD
COLUMBUS, OHIO

OCCUPATIONAL DISEASES
PUBLIC HEALTH PROBLEMS

July 3, 1941

TEL. KINGSWOOD 4841

Dr. Robert A. Kehoe
Kettering Laboratory of Applied Physiology,
University of Cincinnati,
Cincinnati, Ohio

Dear Doctor Kehoe:

Let me spare no words of thanks for your letter of July 1st, although you failed to enclose the reprint you mentioned, or perhaps it is coming in separate mail.

*Separate
mail 7/7/41*

I am very pleased to have your carefully expressed views on the subject of definite standards in relation to the diagnosis and care of men in industrial establishments, and you can rest assured that I agree with you in every way. You will note the cautions I made along this line in the enclosed "Comments on the Diagnosis of Lead Poisoning", the last revision of which appeared in 1936 in connection with my old job at the Ohio Department of Health. I understand the same mineo comments are still being distributed by the Department upon request. Items 3, 4, 5 and 7 would apparently have a bearing on our present discussion.

I am also obliged to you for your evaluation of the term "mean" as you use it and your illustrations for it. I note that Leschke (Clinical Toxicology, 1934, p. 12) undoubtedly agrees with your views, after reciting figures for granulated erythrocytes (P. Schmidt) where he recommends a suggestion by Goetzel and Teleky to use such descriptive terms as "no, few, or many such cells", with some defining explanations.

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RLL*

My discussion of this subject with Dr. Straus has no medicolegal case in point, at least so far as I know, but is purely theoretical or, perhaps one might say, philosophical. I shall certainly insist on his accepting a broad interpretive point of view, but it is my fear that he wishes to administer his new job on a too confined mathematical basis. Personally, I have not heard of him before in this field of work and I note that he is listed in the last AMA Directory as specializing in Surgery. I have a faint impression of knowing him before I left Chicago in 1913. He was a graduate of Rush in 1907 and I think was one of our quiz class masters when we were drilling for the civil service examination for internships in Cook County Hospital in 1907-08. But of course he may be pretty well founded in industrial health matters, including lead poisoning. Happily, discussions of this sort bring us closer together on general agreements, and in the matter at point we have to rely especially upon men with extensive research experience.

Again thanking you, I remain

Sincerely yours,

Emery R. Hayhurst

N 5979

Comments on the Diagnosis of Lead Poisoning

1. Definitions* - LEAD--The element Pb (plumbum), its organic or inorganic compounds or forms, or admixtures thereof or therewith.

LEAD EXPOSURE--Any environmental condition or practice that permits of entry of lead into the body.

PORTALS OF ENTRY FOR LEAD--Refers to the respiratory tract and the digestive tract. Lead may likewise be implanted in the body through direct physical means, by hypodermic injection, or by intravascular administration. With the exception of tetraethyl lead, and related organic compounds, its absorption through the skin or through abraded or lacerated surfaces may be considered negligible.

LEAD INGESTION--When lead enters the body by way of the alimentary tract.

LEAD INHALATION--When lead in a dust, spray, vapor or volatile form enters the respiratory passageways through breathing effort.

LEAD ABSORPTION--When lead enters the body through any portal and is taken into the tissues.

LEAD POISONING or LEAD INTOXICATION--When absorbed lead causes subjective symptoms with objective findings.

CHRONIC LEAD POISONING--When absorbed lead causes protracted manifestations with or without acute episodes.

LEAD COMPLICATIONS--When absorbed lead initiates or aggravates any other disease condition.

LEAD SEQUELA--When a pathologic condition remains as a residuum of antecedent lead poisoning.

2. Blue line in gum margins. Examine after use of tooth brush. Examine both labial and lingual surfaces. The deposit occurs in the papulae of the gum mucosa so that a fine, stippled appearance may at times be seen when a hand lens is used. Is due to lead in the blood stream combining with sulphur in foods. Occurs in about 20 per cent of cases of Leading (Absorption or Poisoning). The condition is less likely to be found where oral hygiene has been good; also when gingivitis or gum atrophy occur (and these latter may be due to the lead deposit). NOTE: A dark line occasionally occurs after medicinal bismuth injections, hence this must be ruled out. Likewise, examine anal muco-cutaneous junction for blue line due to same causes as above.

3. Blood findings. Stippling, polychromatophilia, reticulocytosis, and basophilic aggregation are apparently but gradations of the same picture, according to technique used. These occur more readily in LEADING than in other pathological states. They indicate an increased concentration of lead (or its effects) in the blood stream. Although exceptions occur, they usually remain in the blood as long

*"Lead Poisoning" - Report of the Committee on Lead Poisoning. Amer. Pub. Health Ass'n. (50 W. 50th St., New York, N.Y.). 1930. Price 75 cents.

as exposure to lead persists, and tend to decrease upon withdrawal from exposure, even though the case passes into LEAD POISONING. They may reappear, or increase, during acute episodes in the course of Lead Poisoning. Their number is taken as a rough measure of the amount of exposure (again, with individual exceptions). Hence, workers on the job who show these red cell changes, even without other evidences of leading, should have blood examinations made frequently (preferably weekly), and, advisedly, be removed from exposure on evidence of progressive increase of these cells.

In LEAD EXPOSURE, hazard may be inferred when stippled cells occur to the extent of about 500 per million red cells (5 in 50 average fields), reticulocytosis or basophilic aggregation to $1\frac{1}{2}$ - 2 per cent (of red cells). In general, the larger the granules in stippling, the greater the significance, as indicating excessive absorption of lead.

When LEAD POISONING is definitely established, fluctuating retrograde changes occur in the whole blood picture. The more constant findings are (1) RBC - secondary anemia, disturbed coloring properties, variations in size and shape, and (2) WBC - slight or moderate leucocytosis (increased with infected gums, etc.), slight relative lymphocytosis (changing to lymphocytopenia during acute exacerbations), and mononucleosis.

4. Reports of Analytical Findings of lead in the urine, feces and blood are of doubtful value unless accuracy and delicacy of testing methods are assured, and the patient is under control as to extraneous sources of lead (food, water, tobacco lead-foil, cosmetics, etc.). Also, the test-observations must be made over days and preferably weeks to get a true picture. "Normal lead" probably exists in the amounts of 0.05 to 0.10 mgm. per liter of urine, and to a somewhat higher proportion in the blood.

5. Single or occasional negative laboratory findings do not rule out Lead Poisoning, but positive findings are quite significant. Also, deferred laboratory tests (months after exposure) are usually negative as regards all specific or "characteristic" findings for lead. Here, some have found them to return for a brief period during de-leading treatments.

6. Blood Pressure is subject to wide variations under the influence of lead. Hypotension is more common in early stages, hypertension in longer standing cases.

7. Therefore, the Diagnosis of Lead Poisoning is based upon the weight of certain evidences: (1) Definite exposure to inhaling or ingesting lead or its compounds in amounts equal to at least $1\frac{1}{2}$ to 2 milligrams per day, over 2 or more months' time - less time if greater concentration - and in the form of dust, sprays, molten fumes; (2) objective findings of lead absorption (blue line, blood changes, etc.), neuro-vascular involvements (motor weakness in most used parts, pallor, tension disturbances), and nutritional depletion (especially in chronic cases); and (3) the presence of a number of the subjective phenomena listed, - the more acute cases showing those toward the tops of the two columns. To be occupational, industrial exposure must be established.

STATE OF OHIO
DEPARTMENT OF HEALTH
STATE OFFICE BLDG.
COLUMBUS.

July 1, 1941.

Dr. Emery R. Hayhurst,
Consulting Industrial Hygienist,
1925 Concord Road,
Columbus, Ohio.

Dear Dr. Hayhurst:

I am glad to write in reply to your letter of June 25, and to express my point of view on the questions you have raised. As a partial answer I am sending you herewith a reprint which gives something of my viewpoint.

With respect to the significance of "stippling", it is my feeling that too much attention is being paid to the setting of definite standards in relation to diagnosis and the care of men in industrial establishments. The fact of the matter is that this phenomenon is not specifically related to lead absorption, and it does not bear any definite relationship in the individual to the quantity of lead absorbed except within certain very rough limits. These limits, indeed, are so rough that they do not provide adequate basis for judgment in the individual case. There is no question that groups of normal persons display findings with respect to stippling which greatly overlap the findings obtained in groups of exposed individuals. When one realizes this fact, it is necessary to realize that no amount of juggling of figures will ever answer the problem. If you are presented with the question of the significance of stippling in an individual case, you will have to decide it on the basis of the range of variation displayed by normal persons as well as the range of variation displayed by exposed persons. If the result in point falls within the range where these two sets of values overlap, it must be apparent that no decision can be arrived at on the basis of stippling. Accordingly, in medico-legal cases the number of stippled cells present in the blood has little or no diagnostic value, if it is not clearly above the range seen even in occasional normal individuals.

In this situation it is quite clear the corroborative evidence must be available in order to permit a conclusion to be drawn. It is, therefore, in my opinion, entirely futile for you and Dr. Straus to argue the ques-

tion of what should be the arbitrary standard. Indeed, in my opinion, there should be no arbitrary standard. In the individual case one should take all the facts into consideration and arrive at a judgment which is based on all the facts, rather than on one or two inadequate criteria. With specific regard to the "mean" value, I believe you have misunderstood its implications. A "mean" value, in the sense we have used it, is merely a mathematical expression which, with its probable error indicates the probabilities for the occurrence of results in a sufficiently large universe. Any individual taken at random can fall anywhere within that universe, and so long as this is the case, there is simply no point in arguing whether he belongs in this universe or another. Such argument is truly fictitious. The same is true in the matter of values in the urine. If normal values range between .01 and .19 mg. per liter, then a random observation made on one individual that falls within this range must be accepted as evidence that the individual is normal, unless other additional evidence demonstrates to the contrary.

Returning again to the subject of stippling, I think it is fair to say that those of us who watch men under conditions of industrial exposure set very little value to the actual number of stippled cells. What is important is evidence of a change. If the stippling of an individual workman tends to increase progressively or abruptly, we may look for difficulty. So long as it remains fairly stable, we do not expect trouble. This fact when taken with a known variability of human beings in this respect means that a single observation on the blood of a person suspected of having lead intoxication is of no significance, except as a part of a general picture which is composed of many other facts. The exception to this is that, generally speaking, the absence of stippling is practically conclusive evidence that lead intoxication is not present. In other words, positive results must be looked at very conservatively, while negative results are immediately significant.

I hope this clarifies my opinion on this question.

With kindest regards,

Sincerely yours,

Robert A. Kehoe, M. D.

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TEL. KINGSWOOD 4841

June 25, 1941

Dr. Robert A. Kehoe,
Kettering Laboratory of Applied Physiology,
University of Cincinnati,
Cincinnati, Ohio

Dear Doctor Kehoe:

Thank you very much for your letter and reprints of June 19th, with reference to my letter of June 13th.

I am having something of an argument with Dr. David C. Straus, recently appointed Director, Industrial Hygiene Unit, Illinois Division of Factory Inspection, Department of Labor, concerning the so-called standard of 500 per million (or 5 per 50 average fields) of stippled erythrocytes as the proportion considered significant in inferring lead poisoning.

Dr. Straus cites Dr. Sappington's report of your Virginia paper as published in Industrial Medicine, November, 1940 (p. 558, 2nd column, 1st paragraph) which gives even a lower average of "400 per million in normal persons, the range of variation being 2 to 1000 (80 being the factor for converting the number of stippled erythrocytes from the standard of 50 fields to standard per million)". Dr. Straus correlates this with the statement by Dr. Belknap (Industrial Medicine, October, 1940, p. 506, top of 2nd column), who gives "The so-called normal range of stippled cells" as "from one to 12 per 50 oil immersion fields or from 100 to 1000 per million red blood cells, according to the European standards". (In this, Dr. Belknap is not consistent as you will note from the marked passage in the folder enclosed, entitled "Primer of Lead Poisoning", which was distributed by Dr. Meiter at the exhibit booth of the Wisconsin Employers' Mutuals' at the AMA Meeting in Cleveland earlier this month).

From yours and Dr. Belknap's papers cited above in Industrial Medicine, Dr. Straus states, "The figure 12 per 50 fields figures out to be 960 per million, agreeing with the figure above from Kehoe's paper as being within normal limits". Thus, he appears to accept an occasional maximum as a mean to be generally adopted. Personally, I doubt whether you have meant to discard 400 per million as a generally accepted mean standard for normal. An analogy, of course, is seen in the matter of lead content in the urine where an occasional normal considerably exceeds 0.1 milligram per liter. (Incidentally, I am wondering if, in Dr. Sappington's same report of your Virginia paper, the statement "the mean was 0.97 milligram per liter" is not an error, and that this figure should read "0.097 milligram per liter"?)

In summary, the point at issue between Dr. Straus and myself is whether we should accept 500 per million (or 400 as you mention) for normal persons, or change to 1000 per million, because such may occur as a variation.

I thought perhaps I could get more light on the point by obtaining a reprint of your original Virginia paper, and getting the whole background, and not bother you about it. I had in mind the fact that many errors occur in articles as printed in Industrial Medicine, as you have no doubt noted yourself. For some years I have tried to get Mr. Cloud, the Managing Editor, to forward galley or page proofs for author's corrections, but have never succeeded as far as my own papers have been concerned, and invariably errors have crept in.

My profoundest apologies for detailing all of this to you in the midst of your very busy trestle board, which you state rather modestly no doubt as being "pushed around a great deal" - something which I can well appreciate. - With many thanks, I remain

Sincerely yours,

Emery R. Hayhurst.