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Sender's name and address:

INSTITUTE OF CHILD HEALTH,

GREAT ORMOND STREET,

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July 15, 1964

A. A. Moncrieff
Department of Chemical Pathology
The Hospital for Sick Children, and the Institute
of Child Health
Great Ormond Street
London, England

Dear Sir:

My unfamiliarity with Paediatrics and Paediatricians in your country denies me the privilege of addressing you with a proper salutation, for which, I trust, I may be forgiven. The occasion for this communication is an article by yourself and your associates in British Archives of Disease in Childhood, 1964, 39, 1.

This otherwise splendid article has in it one highly significant conclusion which I believe to be incorrect, and since the point involved is crucial in relation to diagnosis, and even more so in relation to industrial hygiene, I cannot refrain from commenting on it. I have considered it wiser, as well as more courteous, to write to you directly, rather than through a letter to the editor, for my purpose is not to raise an objection as a matter of record, but to invite your comments and more particularly, your search for evidence in support of your expressed view or mine. I shall not subtract anything from my emphasis on this one point, by commenting on any of the other aspects of the physiological and clinical information assembled in this excellent paper. I should say, however, that it is necessary to examine, skeptically, the statements of a number of American authors, with respect to the significance of the analytical findings in the urine, blood and solid tissues, for exactly the same reason that I give in criticising your interpretation of the same data. There is no substitute for direct experience in these matters, and there are very few persons in the United States or elsewhere, who have had such experience.

My point of departure from your position, which is also that of Byers and others cited in the very beginning of your article, relates to (1) the "normal" range of lead in the blood (of both adults and children), and (2) the variability of the levels of the concentration of lead in the blood which are indicative of lead poisoning. The first of these requires little comment, perhaps, although the environmental background of the term "normal" in our day, as in former times, is of more than a little significance, considering the natural opportunities for the absorption of lead, and the ubiquity and variety of the artificial factors in the environment. Concerning the second point, it seems evident that the variations in the concentration of lead in the blood of both adults and children have so impressed themselves upon most of the interpreters of these phenomena as to have obscured almost utterly the facts which emerge when the variability is examined critically in relation to the clinical entity of lead poisoning, and the factor of time. I shall explain in some detail what is meant by the latter part of the last sentence.

There can be no doubt, whatever, that there is a high degree of variability

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in the concentration of lead in the blood. There is also, as the counterpart of this variability, a high degree of variability in the rate of the absorption of lead by persons in our society. These relationships have been investigated in some detail in this Laboratory over the period of many years, and it is important to recognize, in this connection, an extremely important matter. The analytical data so obtained have been furnished by the same persons, employing the same two methods of analysis, in parallel, which have been in use essentially unchanged since 1938. The error associated with the application of each of these two methods has been well defined, so that the data can be given essentially absolute significance in positive and negative terms. The importance of this fact, in relation to the concentration of lead in the blood, is fundamental to the consideration of many of the analytical data which have found their way into the literature from certain other sources, especially those concerned with case reports.

Several practical facts have been established by these means.

1. It is entirely certain that there is no level of lead in the blood which is indicative of lead poisoning. Persons with very high levels up to approximately 1000 micrograms of lead per 100 grams of whole blood, may be wholly free of symptoms (not necessarily free of certain biochemical deviations from the apparently normal range).
2. Conversely, there is a range of concentration, which is wholly incompatible with the onset of illness due to lead. In our experience with adults this is utterly incontestable at this time. No case of lead intoxication in industry has ever been found to occur (at the onset), in our experience, except in association with the concentration of lead in the blood equivalent to or in excess of 80 micrograms per 100 grams. (The exact point, if there is a point rather than a narrow range, is difficult to establish, for the reason that there is, inevitably, a small unknown area within the range of the variability of analytical precision. Thus a single finding of 80 micrograms may be 75 to 85 micrograms, at best, or 70 to 90 micrograms, at worst, in terms of analytical error. Only occasionally, however, is this a matter of practical importance, and then it can usually be settled by multiple analyses.)
3. Our observations of "normal" and sick children, made over the period of more than twenty years, in collaboration with our colleagues in the Department of Paediatrics of this Medical Center, have indicated, beyond reasonable doubt, that the relationships of the concentration of lead in the blood to clinical plumbism in childhood are essentially the same as those in adult life. Children with high levels of concentration of lead in their blood (above the threshold) are not necessarily ill. There seems to be somewhat greater threat of the "triggering" of intoxication in the child than in the adult, but there may well be such a simple explanation of this as that the exposure of the child is shorter and more severe, in quantitative terms of absorption, and is this more difficult to handle, than is that of the adult in the industrial environment. (The fact is, of course, that we do not understand the mechanism by which an "excessive" quantity of lead in the body initiates intoxication.)

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We have never found an exception to the rule that, at the onset of lead intoxication, the blood of the child contains 80 or more micrograms of lead per 100 grams. It is true that certain evidences of plumbism persist (in sufficient intensity to justify the diagnosis on historical grounds), after the concentration in the blood has subsided. It is also true that there are often residual findings induced by organic injury, especially to the central nervous system, which, on the historical basis (and on the fairly unique character of certain neuro-muscular lesions), can be diagnosed as the effects of the absorption of lead in excessive amount. Moreover, certain unpredictable (or so it seems to me) vagaries of the relationships between the concentration of lead in the blood and the "body burden" have resulted from the institution of chelation therapy.

All of the foregoing factors, plus variability in analytical precision in various hands, have entered into reports in the literature in recent years. I have yet to encounter a systematic investigation, in the hands of competent persons whose analytical facilities are above criticism, which has brought out data that are in essential disagreement with any of the statements I have made in the several paragraphs above.

You may suspect, at this point, that I have gone to extravagant lengths in presenting this issue to you. And so I have, if I were concerned only with the problem of diagnosis of lead poisoning. There is, however, a good reason for my concern and this relates to the importance of the concentration of lead in the blood, from the aspect of preventive medicine, in industry, particularly, but also in the general field of environmental medicine and hygiene. If you have examined the data, and the theses in preventive medicine that emerges from the Harben Lectures on "The Metabolism of Lead in Health and Disease," you may realize that this is a very crucial point in the recognition of the danger of plumbism, before any illness or disability appears. The adoption and implementation of this principle in industrial hygiene has served to eliminate, utterly, the occurrence of cases of lead poisoning in a number of industries. Its general application would clean up the "lead trades" in this country. This I have been undertaking to bring about in an appropriate professional manner for many years. At this time considerable progress is being made. This progress could be brought to a standstill, or nearly so, if the principle, itself, were to be regarded, in certain circles as invalid. The application of this principle is costly, initially, in a badly managed (from the aspect of industrial hygiene) industry. It is also troublesome, medically, because it requires understanding, attention to detail, and a thoroughgoing development of professional responsibility, on the part of persons who "do" industrial medicine with their left hands in their "spare time." (I should not like to be quoted in this vein, for reasons which will be evident to you, I believe, and it is for this reason, among others, that I write to you rather than to the editor of the Archives.)

I trust that what I have taken the trouble to say will be of some interest to you and your colleagues in their further investigation of this important and preventable (with some difficulty to be sure) disease of childhood.

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Incidentally, if you or others of your associates would like to have bound copies of the reprints of the Harben Lectures referred to above (and in your article), I shall be pleased to supply them.

Cordially yours,

RAK:vr

Robert A. Kehoe, M.D.

cc - Dr. P. S. I. Barry

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