

In response to a request in a letter from Harold Aaron, M.D., the following line by line criticism is made:

Page 1

Line 2: This line, as written, puts childhood plumbism at the top of the list in the occurrence of lead poisoning within our population. This may or may not have been intended, but it is grossly untrue. Cases of occupational lead poisoning far outnumber cases of childhood lead poisoning, although fatal lead poisoning in childhood certainly outnumbers fatal poisoning in the adult. You had better alter line 2 and continue in lines 3 to 5, inclusive, as follows: "clinical plumbism is seen most frequently among workmen in the lead trades, but the disease is seen in its most serious form among children up to four years of age who live in urban areas of poor housing, in the interior of which paints high in their lead content have been employed in former times and are now likely to be flaking and crazing, or are covered up with paint low in lead. Lead poisoning also occurs among adults in the general population in a variety of situations in which articles, including (infrequently) foods or beverages containing unusual quantities of lead or lead compounds, are introduced into the household - poorly glazed pottery, soldered vessels, leaden pipes, etc."

Line 6: The reference to leaded gasoline is entirely erroneous. No case of lead poisoning in this country has ever been traceable to air pollution with leaded gasoline. The reference to leaded gasoline should be deleted completely. Moreover, air-borne lead compounds, in only the rarest instances, such as in connection with the use of battery cases for fuel in homes of the poor, have been involved in cases of lead poisoning in the general population of this country. Moreover, human lead poisoning has probably never occurred in homes or areas near smelting plants, for the fall-out of lead in the area has affected forage, primarily, and has caused lead poisoning among herbivorous animals when they consume large quantities of contaminated forage. The

flesh (and milk) of leaded cattle do not contain hygienically significant amounts of lead, because of the fact that most of the lead is in the skeleton.

Line 7 (concluding clause): "the greater part by the kidneys" is true only when the dose absorbed into the body is quite minute. Otherwise, the true excretion in the feces is equivalent to, or greater than, that in the urine. It is sufficient here to say "is excreted in the urine and feces." (Most of the lead in the feces is not a true excretion but is, rather, lead which has been swallowed but not absorbed.)

Line 11: The therapeutic use of chelating drugs is not a very effective means of combatting the active symptomatology of lead poisoning in either the child or the adult, and rapid results should not be expected, although they may be at times. Rather, the therapy of reducing the body burden of lead should be in the mind of the physician as a long-term physiologic measure.

Line 15: The pooriness of the housing area is a much more important feature of the background than is mere poverty. It is best to speak of children from an area of poor housing.

Line 16: The stimulus leading to the thorough investigation of a case of illness in the child is the important aspect of the "lead line" in the bones, or stippling of the erythrocytes. These are not specific signs, nor do they confirm a diagnosis. Neither does lead in the blood, above a specific level, prove that any illness is present. There is no level of lead in the blood which is indicative of illness, i.e., is diagnostic. The diagnosis is made on evidence of adequate exposure to lead plus characteristic illness. (I am not splitting hairs here, but rather clarifying a concept which is an essential attitude on the part of the physician.)

Page 2

Line 21: Peripheral neuritis due to lead is rare in these days: Alimentary disturbances, with colic, are much the most frequent manifestation of lead poisoning in the adult. (The term "chronic lead poisoning" has no definitive or accepted

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clinical meaning, and should not be used in discussing the disease of lead poisoning unless it is defined with considerable care.)

Line 24: For clinical purposes, the concentration of lead in the blood is certainly the best available sign of the absorption of lead. An assured increase in the output or concentration of lead in the urine is the earliest sign, but the factors which induce physiological variations are so great as to confuse the issue, except under carefully controlled conditions.

Line 25: There is no assurance that symptoms of lead poisoning will occur at the level of 80 mcg. per 100 grams of blood, nor at any other level. Eighty micrograms is the least level at which the onset of symptoms of lead poisoning has been observed in the lead-exposed child or adult. Lower levels exist later in the illness of either, and considerably higher levels are associated with most of the cases in industry. I have never seen lead poisoning begin to be demonstrable at 60 micrograms. Such cases are seen in hospital practice, because the analyses are not made at the onset of illness, but days or weeks later.

Lines 33, 34 and 35: Delta aminolevulinic acid occurs (usually without evidence of illness) whenever the absorption of lead occurs at a sufficient rate to elevate the concentration of lead in the blood. The correlation involves the concentration of lead in the blood, not the occurrence of illness. The level at which it becomes demonstrable is usually at about 40 micrograms of lead (Pb) per 100 grams of whole blood. The increase in the concentration of coproporphyrin comes later at a higher level of lead in the blood.

Page 3

Lines 43, 44, 45 and 46: These sentences should be deleted entirely. The atomic absorption methods are in use in some of the best laboratories of this country. Spectrographic methods have been used in this Laboratory since 1935. The problem in the small laboratory is the high cost of the equipment. The statement about the

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Measurement of the concentration of lead in "casual" specimens is correct. If one speaks of the urine at all, it should be emphasized that the greatest possible care should be exercised in the collection of the specimen, to make sure that it is not contaminated, and also to make sure that it is a truly representative sample. This actually is a difficult problem. Specimens collected by ordinary hospital techniques are utterly worthless, and worse - misleading.

The discussion of chelating agents is generally satisfactory. It would be better not to go into the matters discussed on pages 1, 2 and 3, down to the "choice of chelating agents" unless they can be done with absolute correctness. There are too many statements that are either untrue or necessarily incomplete.

KE 0019669

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THE MEDICAL LETTER

a non-profit publication

on Drugs and Therapeutics

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ARTHUR KALLET

November 29, 1971

Robert A. Kehoe, M.D.
Kettering Laboratory
University of Cincinnati College of Medicine
Cincinnati, Ohio

Dear Dr. Kehoe:

I am enclosing a copy of an article on "Chelating Drugs in Lead Poisoning," prepared for publication in The Medical Letter.

In accordance with our usual practice, we are sending this manuscript to clinicians and investigators whose criticisms and suggestions would be of special value.

As you may know, The Medical Letter is an independent, non-profit publication the purpose of which is to provide reliable appraisals of drugs for physicians and other health personnel. We will be grateful for your comments, reference to pertinent reports, any suggestions you have and other consultants who might contribute useful information.

In appreciation, we are entering a complimentary subscription to The Medical Letter in your name.

Sincerely yours,



Harold Aaron, M.D.

HA:b
Enc.

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