**DON'T SAY IT—*WRITE IT***

J-5187

To _____ Location _____

From _____ Location _____ Phone No. _____

Subject Chisolm's response to L.A. County. Date 7/8/77

Note that Dr. Chisolm cites need for serial studies and absence of good human data on "subtle impairments".

G-88 REV. 10-62

SAFETY IS A LIFETIME CONTRACT—DON'T CANCEL IT

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8. Albert RE, Shore RE, Sayers AJ, et al: Follow-up of children overexposed to lead. *Environ Health Perspect* 7:33-9, May 1974.
9. Koenig H: FEP studies in normal newborns. To be published.
10. Perkins KC, Oski FA: Elevated blood lead in a 6-month-old breast-fed infant: The role of newsprint logs. *Pediatrics* 57:426-7, 1976.
11. Sachs HK, Blanksma LA, Murray EF, et al: Ambulatory treatment of lead poisoning: Report of 1155 cases. *Pediatrics* 46:389-96, 1970.

*Consultant's reply:* **J. JULIAN CHISOLM, JR., MD,** senior staff pediatrician, Baltimore (Md.) City Hospitals; associate professor of pediatrics, Johns Hopkins University School of Medicine, Baltimore. Dr. Magnus has addressed himself to a difficult and, as yet, unsettled question: At what level of increase in lead absorption are the benefits of chelation therapy likely to outweigh its inherent risks in asymptomatic children? Also, are there other modalities of therapy that carry less risk? Recent studies in experimental animals reveal that nutritional factors are exceedingly important. A high fat intake, as well as dietary deficiencies of calcium, iron, copper, and zinc, increase the absorption and retention of lead in the body.[1,2,3] It may not be generally recognized that the chelating agents used in the treatment of plumbism are not specific for lead. On the contrary, they mobilize and remove substantial amounts of other trace minerals, along with lead, including zinc, copper, and iron. For these reasons, I feel that control of exposure, proper housecleaning, and great emphasis on improved diet provide the most judicious therapeutic approach in the management of children with blood lead concentrations falling between 30-49 μg/dl. It goes without saying that the single most important modality of therapy is the identification of a particular child's source of excessive intake, followed by the prompt separation of the child from that source. It is also true that one needs to determine trends; therefore, serial measurement should be made in such children in order to determine whether their blood lead concentrations either are stable, are falling, or are rising.

The only evidence suggesting that blood lead concentrations in the 30-49 μg/dl range may be followed by subtle impairment in learning and behavior comes from young animals.[4] There is no definitive evidence on this point in children. Most of the reported human studies are retrospective and contain other important defects in design. One of the major deficiencies is the absence of serial blood lead measurements during early childhood.

On the other hand, there is a general consensus that blood lead concentrations above 50-60 μg Pb/dl whole blood signify an unacceptable risk, particularly if associated with clear evidence of derangements in heme synthesis.[4,5,6] One retrospective study in children provides evidence that chelation therapy is beneficial in those children with blood lead concentrations greater than approximately 60 μg/dl.[7]

It is clear that institution of chelation therapy *after* the onset of acute clinical symptoms in children does not uniformly prevent the occurrence of central nervous system sequelae. In my opinion, chelation therapy should be instituted prior to the onset of symptoms if confirmed blood lead levels exceed 50-60 μg/dl. This point may not have been clear in the original article in *Patient Care*. Occasionally, one does see asymptomatic patients who have a very sharp rise in lead absorption associated with very brief exposure. If such brief overexposure can be promptly terminated, then soft tissue lead levels will fall of their own accord without resort to chelation therapy. In most instances, however, overexposure is chronic, and chelation therapy would appear to be indicated.

Dr. Magnus has suggested the more widespread use of the $CaNa_2EDTA$ mobilization test. To obtain meaningful data, one should have timed quantitative collections and access to properly cleaned collection bottles. Such bottles are usually cleaned with nitric acid, followed by copious rinsing with distilled deionized water. In addition, *diagnostic doses* of $CaNa_2EDTA$ should *never* be used in children with clinical symptoms compatible with plumbism; if the symptoms are due to lead poisoning, a single diagnostic dose can exacerbate the illness. Alternate diagnostic tests and full therapeutic courses of chelation therapy should be used, in the hospital, in such patients.

One should be cautious about the outpatient use of chelation therapy. There are now data in animals that indicate that even parenteral administration of chelating agents can increase the absorption and retention of any excess lead that may be present in the intestinal tract.[8] It is my strict policy to give chelation therapy on an outpatient basis *only* after the child has been separated from the abnormal sources of lead and a successful inpatient course has been completed. When using d-penicillamine, I take the additional precaution to give the entire daily dose at 5-6 AM to ensure that the medication is given on an empty stomach. Past clinical experience indicates that outpatient therapy in a child with persistent pica can only make matters worse. Space does not permit a more detailed response. However, the interested reader may find the references listed below of interest.

1. Klauder DS, Petering HG: Protective value of dietary copper and iron against some toxic effects of lead in rats. *Environ Health Perspect* 12:77-80, Dec 1975.
2. Cerklewski FL, Forbes RM: Influence of dietary zinc on lead toxicity in the rat. *J. Nutr* 106:689-96, 1976.
3. Barltrop D, Khoo HE: The influence of nutritional factors on lead absorption. *Postgrad Med* 51:795-800, 1975.
4. Recommendations for the prevention of lead poisoning in children. Committee on Toxicology, Assembly of Life Sciences National Research Council, National Academy of Sciences, Jul 76.
5. Zielhuis RL: Dose-response relationships for inorganic lead. I. Biochemical and haematological responses. *Int Arch Occup Environ Health* 35:1-18, 1975.
6. Zeilhuis RL: Dose-response relationships for inorganic lead. II. Subjective and functional responses—chronic sequelae—no-response levels. *Int Arch Occup Environ Health* 35:19-35, 1975.
7. Albert RE, Shore RE, Sayers AJ, et al: Follow-up of children overexposed to lead. *Environ Health Perspect* 7:33-9, May 1974.
8. Jugo S, Maljkovic T, Kostial K: Influence of chelating agents on the gastrointestinal absorption of lead. *Toxicol Appl Pharmacol* 34:289-93, 1975.