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March 10, 1955

The Journal of the American Medical Association
535 North Dearborn Street
Chicago 10, Illinois

TO THE EDITOR:

The January 22 issue of the Journal contains a report authorized by the Council on Industrial Health and the Council on Pharmacy and Chemistry, entitled "Misuse of Edathamil Calcium-Disodium for Prophylaxis of Lead Poisoning." Some of the viewpoints expressed therein are more controversial than may be apparent to the casual reader. Inasmuch as there are divergent opinions supported by substantial evidence, these deserve to be recorded in the Journal.

Since the report centers around "prophylaxis" of lead poisoning, a definition of prophylaxis is required. In this particular connection, prophylaxis may mean the prevention of lead accumulation, or it may mean prevention of tissue damage secondary to lead accumulation. There is no question that the logical means of preventing lead accumulation is to prevent exposure to lead in absorbable form. Hence, in the present state of our knowledge, administration of any chemical agent for this purpose would truly be a misuse.

On the other hand, in addition to the large number of individuals mentioned in the report who have lead poisoning, there are many more who have laboratory evidence of substantial lead accumulation but may or may not have minor clinical evidence of lead poisoning, such as mild anemia, occasional mild constipation, etc. The prevention of overt symptoms of lead poisoning such as lead encephalopathy, peripheral neuropathy, severe anemia, or lead cramps by reducing existing lead accumulation in these individuals is also prophylaxis. Use of edathamil calcium-disodium ("Calcium Disodium Versenate") for this purpose is not, in my opinion, a misuse of the material. On the contrary, when the industrial physician has been unable to achieve his first objective--namely, the prevention of lead accumulation--his second objective must be the recognition and treatment of the disease as early as possible, preferably before demonstrable tissue damage has occurred.

The report implies that there is no justification for the existence of industrial lead poisoning. Though this may well be true, the practical fact is that lead poisoning continues to exist despite many years of intensive effort to eliminate it on the part of dedicated persons in the medical profession.

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This fact is clearly indicated by the figures quoted within the report. Since lead poisoning does exist, the realistic attitude for a physician must be that it is his responsibility, having done what he can to prevent the condition, to treat it or to prevent its exacerbation.

As the report indicates, there is a substantial evidence of the value of 'Calcium Disodium Versenate' as a therapeutic agent when given parenterally in the presence of existing lead poisoning. This fact is attested by well over 20 publications in the medical literature.

However, the report questions the efficacy of 'Calcium Disodium Versenate' when given by mouth. The bases for this pessimism seem to lie first in the established fact that the material is poorly absorbed from the gastro-intestinal tract, and second, that even though urinary excretion of lead may be increased by the oral use of this material, fecal excretion of lead may be correspondingly decreased. That such a diversion might occur is suggested by a brief abstract report of studies performed in rabbits acutely poisoned by lead acetate. (1) It is apparent that there are major biochemical differences between lead poisoning in rabbits and humans, and also between acute lead poisoning and chronic. That these differences are of critical importance is indicated by the fact that data from 3 different laboratories have now established that there is an overall increase in total lead excretion following the oral administration of 'Calcium Disodium Versenate' to humans with lead poisoning.

Moreover, there is now ample clinical evidence of both objective and subjective improvement in individuals with mild lead poisoning when treated with oral 'Calcium Disodium Versenate'. Such data are found in 3 published articles, (2) (3) (4) in 3 more papers which are currently in press, and in unpublished data from over 20 individual investigators throughout the country. These reports describe subjective improvement which was not duplicated with placebos, and objective improvement as measured by increase in the hemoglobin and red cell count, decrease in stippled cells, increase in urinary lead output, and decrease in blood lead; all of far greater magnitude than that seen in control patients during comparable periods of time.

The report states that "Even if there should be some overall increase in the rate of elimination of lead, the quantities of lead involved in relation to the total quantities absorbed or retained in the body under the conditions of potentially hazardous exposure to lead probably would be too small to be of practical significance."

(1) Rieders, F.: Effect of Oral Na_2Ca Ethylenediamine Tetraacetate on Urinary and Fecal Excretion of Lead in Rabbits, Fed. Proceed. 13:397 (March) 1954.

(2) Sidbury, J.B. Jr.; Bynum, J.C. and Fetz, L.L.; Effect of Chelating Agent on Urinary Lead Excretion. Comparison of Oral and Intravenous Administration, Proc. Soc. Exper. Biol. and Med. 82:226-228 (Feb.) 1953.

(3) Bradley, J.E. and Powell, A.M. Jr.; Oral Calcium EDTA in Lead Intoxication of Children, J. Pediatrics 45:297-301 (September) 1954.

(4) Cotter, L.H.: Treatment of Lead Poisoning by Chelation, JAMA 155:906-908 (July 3) 1954.

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It is true that, at the present time, there is no practical short-term method to free the body of its total burden of lead. However, the symptoms and signs of lead poisoning are produced by a relatively small fraction of the total body lead. It is, therefore, not necessary to render the patient lead-free in order to improve all indices of lead poisoning and to reduce the danger of serious sequelae. It is only necessary to render his soft tissues relatively free from lead. That significant amounts of soft tissue lead can be removed in a reasonably short period of time by means of oral 'Calcium Disodium Versenate' therapy is well established by the extensive experience mentioned above. If this enables the workman to return to his job more quickly and shortens the prolonged absence from work which is commonly required for excretion of soft tissue lead, the result is certainly "of practical significance."

The report also states "Certainly, if a significant increase in elimination were to be achieved, virtually continuous use of the prophylactic agent would be required." I know of no evidence in support of this statement. Furthermore, so far as I know, no responsible person has recommended the continuous use of 'Calcium Disodium Versenate' except as a research procedure under carefully controlled circumstances. On the contrary, the logical approach would be to use this material in courses at intervals to remove accumulated lead.

The report states "When the physician in industry undertakes by medical means to palliate the effects of absorption of demonstrably dangerous quantities of lead by industrial employees, he must look at his reasons for doing so and in all humility and professional integrity ask himself where the welfare of his industrial wards may lie." In full agreement with this statement, I submit that the welfare of his industrial wards resides in removing "the demonstrably dangerous quantities of lead" as rapidly and safely as possible. I submit further that the removal of lead from the body by means of a chelating agent is in no sense of the word "palliation". On the contrary, the treatment of lead poisoning in its earliest recognizable form, which is feasible by administration of oral 'Calcium Disodium Versenate', is in my opinion, consistent with the highest ideals of the medical profession.

In summary then, it is my opinion that substantial published and unpublished evidence demonstrates the efficacy of 'Calcium Disodium Versenate' when given by mouth to remove lead. Second, that any safe and effective means of removing lead from the body is a direct and logical approach to the treatment of lead poisoning, whether diagnosed by symptoms or by laboratory evidence of lead accumulation. Third, that the use of 'Calcium Disodium Versenate' to remove lead from an individual who has been shown to have absorbed "demonstrably dangerous quantities of lead" should not be condemned as "misuse" simply because previous methods have failed.

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And fourth, to condemn the use of a chemical agent to remove lead on the basis that this might encourage laxity in the prevention of lead accumulation seems to me to be analagous to arguing that penicillin should never have been made available because it makes the cure of venereal diseases too easy, and thus encourages promiscuity. Both concepts may be true but are scarcely proper decisions for the physician who is called upon to care for the ill or potentially ill.

Sincerely Yours,

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