

for and the utility of the statement that "the lead-mobilization test indicates a high body burden of lead if the urine level doubles." Does the author mean that a rise from 0.05 $\mu\text{mol/d}$ to 0.10 $\mu\text{mol/d}$ (to convert to micrograms per 24 hours, multiply by 207.21) is a positive test result? This would lead to an erroneous conclusion. Both lead excretions are within the normal limits and, in fact, the difference between the 0.05- $\mu\text{mol/d}$ and the 0.10- $\mu\text{mol/d}$ level may well be within an expected daily variation in lead excretion. Except for when renal insufficiency is clinically apparent, the threshold of 2.90 μmol of lead per gram of edetate per 24 hours of collection is the generally accepted threshold for indicating an elevated body burden.⁸

Dr Rempel recommends that "chelation therapy should be reserved for those with significant symptoms or signs of toxic reactions [italics added]." Readers are then directed to Table 1 of the article for a list of symptoms associated with toxic reactions. This cautionary statement is very justified, but it does not go far enough. It must be stressed that the clinical judgment of a physician properly qualified in occupational medicine and internal medicine is essential for the correct initial diagnosis, for evaluating the indications for the lead-mobilization test, and for weighing the possible risks and benefits of each subsequent episode of chelation therapy.

Edetate or penicillamine both have potential toxicity, as noted by Dr Rempel and others.¹⁴ These therapies also have other limitations. Studies are lacking that show documented improvement of chronic neurological morbidity with their use in asymptomatic persons, especially for mild intoxication.⁴ Additionally, there is a theoretical risk of exacerbation of lead toxicity with chelation therapy via mobilization of lead from the bone compartment and redeposition of a bolus of lead in the nervous system or in the kidneys.⁵ Cory-Slechta et al⁶ showed increased deposition of lead in the nervous system in the initial day of a 5-day course of chelation therapy in rats. Furthermore, many adults with occupational lead intoxication via solder manufacture, smelting, or scrap metal recycling may have also been exposed to other heavy metals such as cadmium. Use of edetate calcium disodium is contraindicated in cadmium intoxication.⁶

Finally, Dr Rempel gives guidelines for the edetate disodium calcium lead-mobilization test using 30 mg/kg, up to a maximum of 2 g. Edetate disodium calcium lead mobilization with an upper-limit maximum of 1 g also has been

used,⁸ and it is not clear from Dr Rempel's article why a higher, 2-g maximum dose should be preferred. Given the concern about edetate disodium calcium's toxicity, a total 1-g challenge should be considered an acceptable maximum dose for the lead-mobilization test.

Robert J. Nadig, MD, MPH
The New York City Poison
Control Center

1. Rempel D. The lead-exposed worker. *JAMA*. 1989;262:582-584.
2. Klaassen CD. Heavy metals and heavy metal antagonists. In: Gilman AG, Goodman LJ, Rull TW, Murad F, eds. *The Pharmacological Basis of Therapeutics*. 7th ed. New York, NY: Macmillan Publishing Co Inc; 1986:1610.
3. Oliver LD, Mehta R, Barles HE. Acute renal failure following administration of ethylenediamine tetraacetic acid (EDTA). *Tox Med*. February 1984;80:40-42.
4. Chisolm JJ Jr. Mobilization of lead by calcium disodium edetate: a reappraisal. *AJDC*. 1987;141:1256-1257.
5. Cory-Slechta DA, Weiss B, Cox C. Mobilization and redistribution of lead over the course of calcium disodium ethylenediamine tetraacetate chelation therapy. *J Pharmacol Exp Ther*. 1987;242:804-818.
6. Friberg L, Piscator M, Nordberg OF, Kjellstrom IN. *Cadmium in the Environment*. 2nd ed. Cleveland, Ohio: CRO Press; 1974:79-80.

In Reply.—As indicated in the original article, the details of the therapeutic and diagnostic chelation presented represented one approach to chelation and the approach that we use at the University of California, San Francisco. Unfortunately, controlled and prospective studies that have evaluated various treatment protocols are lacking. Until such studies are done, there will be no single approach to chelation.

The edetate disodium calcium lead-mobilization test is a measure of total body burden of lead and is used in situations where symptoms of lead toxic reactions are more pronounced than would be expected based on the blood lead level. This situation may occur when blood lead levels are in the approximate range of 1.45 to 3.40 $\mu\text{mol/L}$, levels that correspond to higher 24-hour urine lead levels than presented in Dr Nadig's hypothetical example. Dr Nadig is correct in stating that doubling of very low 24-hour urine lead levels should not be considered a positive test result. In general, we agree with Dr Nadig and prefer to use the threshold of 2.90 μmol of lead in the 24-hour urine collection to indicate a positive test result.¹

The recommended dose for the edetate disodium calcium lead-mobilization test of 80 mg/kg to a maximum of 2 g has been widely used¹⁴ and in a large case series has been found not to be nephrotoxic.⁶ However, as indicated in Dr Nadig's letter and in the original article, chelation is not risk free and the interpretation of the results may be controversial. Therefore, if chelation is considered, it is important to involve clinical physicians who are properly qualified in occupational medicine or toxicology and who have experience with chelation.

Although necessary, it is unfortunate that in the medical literature we tend to focus on the details of the treatment of lead poisoning. From the standpoint of public health, we should be focusing on prevention.

David Rempel, MD, MPH
University of California,
San Francisco

1. Emmerson BT. Chronic lead nephropathy: the diagnostic use of calcium EDTA and the association with gout. *Australas Ann Med*. 1968;12:310-324.
2. Emmerson BT. Chronic lead nephropathy. *Kidney Int*. 1973;4:1-5.
3. Wedeen RP, Mellick DK, Batuman V. Detection and treatment of occupational lead nephropathy. *Arch Intern Med*. 1979;139:53-57.
4. Batuman V, Maesaka JK, Haddad B, et al. The role of lead in gout nephropathy. *N Engl J Med*. 1981;304:520-523.
5. Wedeen RP, Batuman V, Landy E. The safety of EDTA lead-mobilization test. *Environ Res*. 1983;30:58-62.

CORRECTION

Financial Disclosure.—James D. Cherry, MD, has notified THE JOURNAL that the following information was inadvertently omitted from his signed financial disclosure statement that accompanied the submission of his editorial entitled "Pertussis Vaccine Encephalopathy: It Is Time to Recognize It as the Myth That It Is," published in the March 23/30 issue of THE JOURNAL (1990;263:1679-1680). Dr Cherry's financial disclosure should have read as follows: "During the past 6 years, I have received grants and contracts from Wyeth and Lederle laboratories to carry out studies related to pertussis and pertussis immunization. Since 1986 I have also been a consultant to Lederle Laboratories to assist in their acellular pertussis vaccine development program."

Editorial Note.—Since October 18, 1989, THE JOURNAL¹ has required authors of manuscripts published in JAMA to sign the following financial disclosure statement:

I certify that I have no affiliation with or financial involvement in any organization or entity with a direct financial interest in the subject matter or materials discussed in the manuscript (eg, employment, consultancies, stock ownership, honoraria), except as disclosed in an attachment. Any research or project support is identified in an acknowledgment in the manuscript.

This requirement is included in the Instructions for Authors, published monthly.

When appropriate, notices of financial disclosure are published as part of the article so that readers may be aware of possible biases the authors may have, although the editors recognize that reliable, valid work can be done by authors despite conflicts of interest. The editors rely on information provided by authors in response to the above statement. If it is subsequently determined that an important financial disclosure was incomplete or inaccurate, a Correction or Letter may be published to provide accurate information.

1. Lundberg GD, Flanagan A. New requirements for authors: signed statements of authorship responsibility and financial disclosure. *JAMA*. 1989;262:2003-2004.