the United States leaves 2.9 million. By estimating (conservatively) that 50 percent of them would decline participation in a government-sponsored survey, an additional 1.5 million are excluded. This leaves 22.4 million to 23.8 million people, nearly 10 percent of the U.S. population, who are not represented in the sample. The National Cancer Institute estimates that there are currently 8.9 million victims of cancer in the United States, or 3 percent of the population.[2]

We know little of the ecology of this unrepresented decile. However, it is probably quite different from that of the general population. For instance, more than a third of the migrant workers in California reported that they had never seen a physician in their entire lives.[3] My intent is not to criticize the authors' methods but rather to call for comprehensive investigation of the ecology of health care of this population that has been, literally, decimated.

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The authors reply:

To the Editor: Smith appropriately points out the limits of telephone surveys. We concur with his claim. For this reason, we based most of our analyses on the Medical Expenditure Panel Survey, which relies on personal interviews conducted in a nationally representative sample of U.S. households. We also agree that we know less about the people who lack a home address. However, we are unaware of surveys or other information sources that provide reliable data on health care utilization in a nationally representative sample of homeless or migrating populations. Were such data available, the ecology model could be applied to these populations, perhaps constructively quantifying health care disparities that matter.

We share the concern of Goldberg and Goldfrank about potential misuse of our findings to overemphasize or underemphasize the importance and role of particular segments of the health care system. Apparently, they derived from our results an estimate of 43 million emergency visits per year by assuming that each person who visited an emergency department in a single year did so only once. The resulting estimate would be the smallest possible number of visits to emergency departments by those persons during the year. We reported findings based on the number of individual persons involved in a particular type of health care in a month, not their total number of visits or encounters during the month. It is well known that the same individual persons revisit emergency rooms. This is one explanation for the larger number of visits to the emergency department in a year as reported in the National Hospital Ambulatory Medical Care Survey. As pointed out by Smith, higher rates of health care utilization by people who were excluded from the surveys we analyzed, such as prisoners, could be another explanation. Thus, we believe our estimate of the number of people obtaining care in an emergency department in an average month is actually consistent with estimates of annual visits reported in the National Hospital Ambulatory Medical Care Survey.

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Chelation Therapy in Children Exposed to Lead

To the Editor: Rogan et al. (May 10 issue)[1] conclude that chelation therapy with succimer for children with lead levels of 20 to 44 μg per deciliter is valueless. However, an important methodologic weakness of their study is that succimer therapy failed to achieve a timely, enduring reduction in the lead level, producing a difference in blood lead levels between treatment groups of only 2.7 μg per deciliter over a one-year period. There is no evidence (e.g., measurement of erythrocyte protoporphyrin) that succimer effected any significant reduction in the body burden of lead. The authors assert without reference that there is no better chelator than succimer. However, efficacy has been reported with penicillamine[2-4] and with 2,3-dimercaptopropane-1-sulfonate.[5] Finally, the authors ignore the other toxic effects of lead poisoning that can be reversed by chelation — e.g., normalization of 1,25-dihydroxyvitamin D, δ-aminolevulinic acid dehydratase, and erythrocyte protoporphyrin activity.[6] Collectively, these shortcomings leave open the possibility that individualized case management for children with lead poisoning may have a role in treatment, which may in some cases include chelation therapy.

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in treatment of lead poisoning in children. J Pharm Exp Ther 1985;235:665-9.
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To the Editor: Rogan et al. cite a meta-analysis by Pocock et al.[1] demonstrating the association between increased blood lead level and decreased IQ. They do not, however, reveal the conclusion of the authors of the meta-analysis: "However, the inherent limitations of observational epidemiology in pinpointing the reasons for this association mean that uncertainty remains as to the real impact that lead makes on children's neuropsychological development."

Given this uncertainty, a very reasonable explanation for the findings in the study by Rogan et al. — i.e., that lowering blood lead levels did not improve scores on tests of cognition, behavior, or neuropsychological function — is that lead exposure was not responsible for impairment in the first place. This possibility was not even broached by the authors.

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The authors reply:

To the Editor: Shannon et al. propose the use of other oral chelating agents and the treatment of biochemical responses to lead exposure. We evaluated the use of penicillamine when we planned our trial and came to the same conclusion that the American Academy of Pediatrics did: "The overall toxicity profile of penicillamine relegates it to a third-line agent, indicated only when unacceptable reactions have occurred to succimer and CaNa2EDTA."[1] We are not aware of any controlled, long-term data on the reduction of any measure of lead exposure by penicillamine. Concurrent, preferably randomized controls are necessary because of the strong effects of age on blood lead levels, as seen in our study. Similarly, studies showing the efficacy of chelation for protoporphyria[2] and abnormalities of vitamin D metabolism[3] have not been randomized, controlled trials, and their results are consistent with regression to the mean or spontaneous resolution as the blood lead level falls. As for 2,3-dimercaptopropane-1-sulfonate, it is not commercially available in the United States.

Mandelbaum is of course correct in saying that if lead does no damage, then treating lead exposure will do no good. For the purposes of both public health and clinical trials, however, we think that the debate about whether lead causes cognitive deficits at relatively low levels of exposure is settled. Major organizations, including the Centers for Disease Control and Prevention[4] and the World Health Organization,[5] treat the association as causal. Lead is the best studied of the environmental chemical agents thought to produce cognitive deficits at commonly encountered levels, with a huge clinical and laboratory literature showing unquestionable neurotoxicity. The only question is the dose at which the toxic effects become measurable. The relation between lead and neurotoxicity was sufficiently established that we and our advisors thought that a trial attempting to reduce or prevent lead-associated cognitive deficits by means of chelation was needed, and we still believe that to have been true.

We note with sadness the death of our senior colleague, J. Julian Chisholm, Jr., on June 20, 2001.

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FOR THE TREATMENT OF LEAD-EXPOSED CHILDREN
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Acquired Bleeding Diathesis in a Patient Taking PC-SPES

To the Editor: PC-SPES is a commercially available nutritional supplement containing eight herbs that is used by many patients with prostate cancer. It has potent estrogenic activity and substantial antineoplastic effects in patients with prostate cancer.[1,2] We describe a patient with profound bleeding diathesis after one month of unsupervised use of this compound.

A 62-year-old man with hormone-refractory prostate cancer and nodal metastases (stage D1 disease) presented to the emergency department after an episode of syncope. This episode had been preceded by one day of epistaxis, abdominal pain, hematuria, and the passage of maroon stools. The patient denied a family history of bleeding or bruising, and the prothrombin time and activated partial-thromboplastin time had previously been normal. The only medications were 12 capsules of PC-SPES daily (twice the manufacturer's recommended dosage) for one month, in addition to multivitamins. The initial vital signs were notable for a pulse of 120 beats per minute and a blood pressure of 112/82 mm Hg. Physical examination revealed extensive ecchymoses, and a computed tomographic scan showed a large retroperitoneal hematoma. The results of laboratory analysis and mixing studies with normal plasma are shown in Table 1. Hepatic-function variables were within normal limits. Initial treatment included the transfusion of 2 units of packed red cells and 6 units of fresh-frozen plasma and the adminis-

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