Letters

EPA Review of Lead Study

I would like to comment on the recent article by Eliot Marshall (News and Comment, 25 Nov., p. 906) dealing with the dispute between myself and the Environmental Protection Agency (EPA) review panel headed by Lester Grant.

A subject as important as the effects of lead on the health of children deserves careful scrutiny, and I have welcomed and received close examination of my data by responsible scientists. Although I felt that the panel set up by Grant circumvented the peer review process that EPA had established for the Lead Criteria Document, I welcomed them and gave them unlimited access to my data. Grant and I agreed that I would be given a timely draft copy of their report before its promulgation in order to correct any errors of fact. When the visiting team arrived, on 30 March 1983, I presented them with all of the bound printouts of the study and an index to the data; I also provided them with a meeting room. I met with them for two consecutive days to answer their questions. At their request, certain portions of the printouts were photocopied so that they could work with the data sets individually. At the end of May, when the report had not been sent to me, I called Grant's office to ask for a copy of the draft. I was told it was being worked on and that I would receive a copy as soon as it was ready. I continued to request the draft report at monthly intervals until September without effect. On 30 September, at the same time that a copy was sent to the EPA press in Cincinnati for publication, a copy was sent to me. On first reading, I found at least 12 errors of fact; almost all were biased against the conclusions drawn by my study. By express mail, I informed Grant that, if the erroneous report was not withdrawn, I would insist that a complete errata sheet be sent to every recipient, with an acknowledgment that my original agreement with him had not been fulfilled. The report was withdrawn from the printers.

The report incorrectly assigned dentine lead levels to my groups, incorrectly stated the type of dental tissue analyzed, incorrectly labeled the type of IQ test we employed, and incorrectly cited IQ scores. Some of these errors were not of major magnitude but were indicative of the care with which the report was assembled and edited. A few errors were serious, however, and questioned the integrity of my data, myself, and my coworkers. I was startled, upon finding these errors, to realize that three which appeared in the draft document had been pointed out earlier by me in written communications to Grant, on multiple occasions.

The report stated that the rate of mistakes my colleagues and I committed in transferring data from the code sheets to the computer was 7 per 1000. The actual rate was lower by an order of magnitude: 7 per 10,000. This error appeared in the report despite the fact that I had brought it to Grant's attention in writing. It was also stated in the report that I did not furnish the distribution of lead levels across excluded subject groups, which suggested that a source of bias could have entered the study at this point. Actually, at Grant's request, I had sent him complete listings of all the dentine lead levels cross-tabulated by exclusionary class. These tabulations, which the report said I had not furnished, were cited in its bibliography!

One member of the panel is quoted by Marshall as saying that "[t]he basis for excluding certain children is still not totally clear." Yet the reasons were delineated in our original paper (*1*), and the visitors were given copies of the tables listing the excluded subject and the criteria applied. Another panel member stated that, because the computer program "kicked out" cases for which some covariate data was missing, the actual subject number for some of our analyses was less than 158. This is true. It is not true, as he stated, that because the N was reduced, the differences may not have been statistically significant. The program we employed (Statistical Package for the Social Sciences) calculated the P values on the basis of the number of cases actually analyzed, not the number of cases in the data file.

The most serious criticism of my work was the charge that I may have known the lead classification and outcome scores of my subjects at the time I excluded subjects from the study for reasons such as head injury. Had this been true, an important source of bias could have crept into the subject selection. My associates and I took particular pains to prevent this from happening. The report was incorrect, despite the fact that our blinding procedures had been brought to the attention of Grant and the panel on four occasions, twice in oral presentations and twice in written correspondence. While this statement and the others were withdrawn in the final document, the conclusions drawn from them were allowed to stand.

Finally, Marshall indicates that, according to Grant, I became uncooperative when "problems turned up" and asked all of the reviewers to return all the data before leaving his office. This is simply not true. Grant asked if I would allow them to take the photocopies I had provided them back to North Carolina. I asked him whether their confidentiality would be shielded if I gave them to him. He said they would not. I said that, since these data represented work still in progress, they could not take them from the hospital but they could spend as much time as they wished with the data in Pittsburgh.

Eight days after the panel visited me in Pittsburgh, I received a letter from Grant, in which he wrote:

> Thank you for taking time out of a busy schedule to meet last week with myself and members of the expert committee that I have asked to review your studies on association between neurobehavioral effects and low level lead exposures in children. Your assistance in providing an introductory overview of your studies, in making computer printouts of data and statistical analyses results available for inspection by the committee, and in answering questions posed in regard to procedures employed in collecting the data and analyzing the results of your studies was quite helpful and appreciated by us, as was the assistance provided by your secretary during our visit.

It is not clear to me why there is a disparity between these two statements by Grant.

I have never claimed that my work is flawless. Epidemiology in the real world does not permit such hubris. It is, however, more than a little frustrating to see refractory misinterpretations of fact and inference applied to it in the face of repeated efforts at correction.

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1. H. L. Needleman *et al.*, *New Engl. J. Med.* **300**, 689 (1979); _____, A. Leviton, D. Bellinger, *ibid.* **306**, 367 (1982).

Marshall reports on criticisms directed against the pediatric lead studies of Needleman *et al.* by consultants to EPA.

Needleman *et al.* (*1*) evaluated the neuropsychologic performance of 58 children with high dentine lead concentrations and of 100 children with low concentrations. The children with the high lead concentrations achieved a mean IQ score on the Wechsler Intelligence Scale for Children which was approximately four points below that of the children with low concentrations. Analysis of variance indicated that this difference could not be explained by any of 39 covariates, such as age, sex, race, socioeconomic status, past medical history, or child-rearing practices. Needleman *et al.* (*2*) demonstrated subsequently that the downward shift in IQ was associated with a significant reduction in the number of children in their high lead group with IQ's above 125 and with a trebling in the number having IQ's below 80. These findings have been generally corroborated in studies by Ernhart *et al.* (*3*), Lansdown *et al.* (*4*), Winneke *et al.* (*5*), and Smith *et al.* (*6*). A recent review by Rutter (*7*) concluded that those studies of the association between lead and IQ in which close heed has been paid to methodologic issues have consistently found a dose-response association between lead exposure and neuropsychologic deficit. This effect appears to have been indisputably established at blood lead concentrations above 40 micrograms per deciliter, and there is growing evidence to suggest that, even at lower concentrations, lead can cause a subtle, but irreversible, reduction in children's intelligence.

Atmospheric lead emissions have increased 2000-fold since the pre-Roman era, and even then the atmosphere may have been contaminated with lead by a factor of 3 over natural background (*8*). In 1978, the second National Health and Nutrition Examination Survey (*9*) estimated that 660,000 children age 6 months through 5 years in the United States had blood lead concentrations above 30 micrograms per deciliter, the concentration considered by the Centers for Disease Control (*10*) to represent excessive lead absorption. Taken together with the data of Needleman *et al.* (*1, 2*), these findings have profoundly disturbing implications, not only for the future development of the affected children, but for the whole fabric of modern American society. Fortunately, the number of children in the United States with acute high-dose lead poisoning has declined precipitously during the past decade as the result of implementation of the Lead-Paint Poisoning Prevention Act. Also the background rate of pediatric lead absorption has been reduced substantially, most likely as a result of the EPA-mandated phasedown in the lead content of gasoline (*11*). This latter accomplishment is, in no small measure, a consequence of Needleman's work.

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5. G. Winneke *et al.*, in *ibid.*, pp. 249–266.
6. M. Smith *et al.*, *Dev. Med. Child Neurol.* **47** (Spec. Suppl.) (1983).
7. M. Rutter, in *Lead Versus Health*, M. Rutter and R. R. Jones, Eds. (Wiley, New York, 1983), pp. 333–370.
8. M. Murozomi, T. J. Chow, C. Patterson, *Geochim. Cosmochim. Acta* **33**, 1247 (1969).
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10. Centers for Disease Control, *J. Pediatr.* **93**, 709 (1978).
11. J. L. Annest *et al.*, *New Engl. J. Med.* **308**, 1373 (1983).

With Marshall's report, we finally have an independent published report, in an important journal, of criticism of the "classic" Needleman study of lead effects. Some of the problems identified by the Expert Committee on Pediatric Neurobehavioral Evaluations appointed by EPA have been mentioned in my public statements. Other problems, such as biases associated with missing data, were barely discernible in the published reports and are now substantiated through the committee's limited access to the data.

Since my role as adversary is mentioned, I would like to clarify a few points. Needlemen attributes criticisms of his work to industry affiliation; however, at the time of the first publication (*1*) in which I refer to problems in his work, I had no connection with the lead industry. (I now have a modest research grant from the International Lead Zinc Research Organization.)

Marshall states that I have maintained "that there is no proof of a causal relationship between high levels of lead in children's blood and low scores on IQ tests. . . ." This is misleading. There is a definite and tragic risk of intellectual deficit associated with *high* levels of exposure, and I have never stated otherwise. My assertion is that there is no convincing evidence of an association of low level lead exposure and measurable deficits in psychological development when other relevant factors (such as parent intelligence, home environment, and so forth) are controlled. Unfortunately, efforts to blame the problems of many of our disadvantaged children on lead exposure tend to detract our attention from the amelioration of the difficult conditions in which these children are reared.

My "docility" about the committee's findings results from a respect for the competence and courtesy of its members and a recognition of the validity of the major features of its review. My associates and I cooperated in supplying EPA with complete sets of our data. We also conducted reanalyses as requested. (An additional reanalysis has since been requested.) The corrected results did not support the conclusion that low level lead exposure is related to deficits in intelligence. This applies to the earlier work mentioned by Marshall, as well as the data from the 1981 report. The sample sizes, however, do not provide the statistical power necessary for a reasonably definitive statement that there is little or no effect.

Recent, well-controlled studies (*2, 3*) in the United Kingdom also failed to support the Needleman position. One study (*3*), directed by Marjorie Smith, is particularly important because it replicated Needleman's procedures with a large sample and sound methodology. After appropriate control of confounding variables, no significant association of dentine lead and intelligence was found.

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3. M. Smith, T. Delves, R. Lansdown, B. Clayton, P. Graham, *The Effects of Lead Exposure on Urban Children: The Institute of Child Health/Southhampton Study* (Department of the Environment, London, 1983).

Erratum: In the Research News article "New test of variable gravitational constant" (23 Dec., p. 1316), in the third paragraph of column two on page 1317, a minus sign was left out of an exponent. The correct value for the drift of atomic clocks relative to gravitational clocks is $(0.1 \pm 0.8) \times 10^{-11}$ per year.