COMMENTARY
The Landmark Needleman Study of Childhood Lead Poisoning: Scientific and Social Aftermath

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The 1979 landmark study of Needleman and colleagues first established that low levels of lead in children produce asymptomatic but significant, persisting neurotoxicity measured as cognitive and behavioral dysfunctions. Numerous cross-sectional and longitudinal human studies, animal studies, and mechanistic investigations have since confirmed and expanded upon Needleman's results to yield a coherent, converging whole. The 1979 study also opened a new volume of socioscientific thinking on this ancient problem. Subtle lead neurotoxicity in children means IQ decrements in 3 to 4 million U.S. children and in many more millions elsewhere. In the aggregate, an enormous cognitive deficit across U.S. society has occurred and will continue. The study provoked questions. What is an adverse health effect and who defines it? What is the relative importance of population-wide versus individual toxic insult? What are the roles of clinical intervention and preventive medicine? What are the tradeoffs between social costs of injury to children's brains and economic costs of preventing exposure?

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Elsewhere in this issue of the *Quarterly* [1], Herbert Needleman presents some of the issues surrounding childhood lead poisoning, including a brief historical perspective and a summary of his landmark study on childhood lead poisoning [2]. His original study and its 11-year follow-up [3]

showed that low levels of lead in the bodies of very young children produce persisting neurotoxic effects, including full-spectrum IQ deficits and other neurobehavioral disorders.

The 1979 Needleman et al. study initially provoked an unprecedented level of scrutiny and even hostility from certain economic, health policy, regulatory, and scientific quarters. More importantly, however, the Needleman study also helped to provoke an enormous amount of research into lead exposure and toxicity in children and other risk groups, animal models of lead toxicity, and mechanistic studies of lead's toxic actions. The 1979 study also elevated lead to the status of prototype for reworking fundamental risk assessment perceptions and assumptions about environmental health injury in America and elsewhere.

A CHALLENGE TO CONVENTIONAL CLINICAL THINKING

The 1979 Needleman study forced a rethinking of the conventional toxicological and biomedical definition of childhood lead poisoning, a definition based on clinical signs and symptoms. While it is true that, some decades before, Byers and Lord [4] had found neurobehavioral sequelae to the early severe, fulminant manifestations of lead poisoning, these sequelae were still rooted within "clinical lead poisoning," i.e., involved relatively high body lead burdens in the poisoned children. Needleman's psychometric subjects had no clinical history of lead poisoning treatment; such a history, in fact, constituted one of the exclusionary criteria in the study. The Needleman study therefore set the stage for accepting lead "poisoning" as including subclinical or asymptomatic intoxication. As new evidence has continued to become available, such an interpretation continues to extend lower and lower into human lead exposures once considered "safe."

In sparking a redefinition of lead poisoning, the Needleman study challenged the role of the clinician in the overall societal response to lead poisoning as a health problem. The clinician obviously retains the role of medical manager in cases of overt, classic lead poisoning in individual patients. If lead poisoning also exists in groups of children who are otherwise asymptomatic by traditional clinical criteria, however, where is the clinician's role? The role in this case is increasingly one of evaluating toxicity *risk*, i.e., judging level of neurotoxicity *risk* given some index of lead exposure such as blood lead (Pb-B) concentration and such guidance as the periodic Statements of the U.S. Centers for Disease Control (CDC) or Statement-linked pronouncements from organizations such as the American Academy of Pediatrics [5–9]. Contrary to a widespread perception in the scientific and biomedical communities, a CDC Statement on childhood lead poisoning is a categorical depiction of risk via screening results; it is not meant to serve a surrogate diagnostic function.

The changing role of the clinician in childhood lead poisoning as a broad health problem is mirrored in the changing nature of CDC Statements since the Needleman study. In the 1975 [5] and 1978 [6] Statements, federal and independent advisory physicians defined risk categories in the clinical portion of lead's toxicological spectrum, with remedies also rooted in medical intervention and management. In CDC's 1985 Statement [7], however, there is both the clear "official" acceptance of asymptomatic or subclinical lead poisoning as a bona fide aspect of the disease and the first inklings of a sharing of roles between the medical manager and the preventive medicine specialist, the latter through environmental control measures.

The 1991 CDC Statement [8] formally stratifies lead poisoning into multitiered definitions and categories, only the most severe of which apply to traditional clinical management of lead poisoning. The Statement assigns clear and substantial roles for preventive environmental medicine. In its explicit attempts to recognize lead poisoning as a multidisciplinary problem and to take it beyond the exclusive province of the pediatrician, the Statement is bound to produce further debate in the pediatrics community, particularly in that segment that is uninformed or only marginally informed as to the great advances taking place in the area of lead research.

THE NEEDLEMAN STUDY'S PUBLIC HEALTH IMPACT

The public health impact of the Needleman study is best understood in context. The federally funded Needleman et al. study appeared at the end of a decade that first saw formalizing of legislative, administrative, and judicial acknowledgments that environmental protection and pollutant-affected

health protection were appropriate and necessary public functions. In 1970, the U.S. Environmental Protection Agency (EPA) was formed, and, in the 1970s, the National Institutes of Health began to fund extensively lead research of independent scientists such as Needleman and colleagues through competitive, peer-reviewed grants.

The U.S. Surgeon General issued a major statement on lead toxicity in 1971, identifying a lower Pb-B threshold as toxic and calling for large-scale systematic screening, a call taken up by the U.S. CDC in its 1975 and 1978 Statements (see above). Congress began a series of legislative initiatives in 1970 with the 1970 Clean Air Act and its 1977 amendments and the 1971 Lead-Based Paint Poisoning Prevention Act. The U.S. EPA in 1977 produced the first of its two benchmark documents on environmental lead exposure and toxicity [10] at the same time that the World Health Organization (WHO) published its first criteria document on lead [11].

Needleman's 1979 work was not only a major result of the slowly growing shift in how lead as a public health issue was approached, it was establishing in turn the mainstream of later thinking. As such it served as a key link to the next generation of international research, regulatory, and public health policy efforts that took place in the 1980s and that continue to the present

In fostering a broad expansion of the definition of lead poisoning, the Needleman study helped to produce a qualitative and quantitative change in perception of the lead problem. When clinical lead poisoning was held to be a problem of inner-city, impoverished areas quantifiable by case finding, the problem was seen as one managed by secondary/tertiary prevention measures: find poisoned children and treat them. Shifting the definition of lead poisoning to asymptomatic children had various effects. One effect was obviously to invalidate the traditional approach for other than overt poisonings identified via screenings. A second effect was to broaden greatly the definition of the socioeconomic and demographic profile for a lead-poisoned child. The profile not only included impoverished, inner-city children but suburban children of affluent families as well. This can be seen in the U.S. Agency for Toxic Substances and Disease Registry's (ATSDR's) Report to Congress on U.S. childhood lead poisoning [12]. While inner-city, low-income children have the highest prevalences of elevated, toxic Pb-B levels, the larger numbers of non-inner-city, non-low-income children in the U.S. population meant that even lower prevalences translated to unacceptable total numbers of lead-exposed children.

The ATSDR report noted that 2.4 million metropolitan black and white children under six years old had toxic Pb-B concentrations (>15 μg/dl) in 1984. The present EPA prevalence estimate for the new CDC toxic Pb-B definition of 10 μg/dl is about 15%, yielding a national number of children (aged under six years) of over 3 million [13]. Most of the decline in source lead has already occurred, and it is not likely that declines in child lead intake rates in the 1990s will be anything like the major declines of the 1980s without major lead abatement policy changes and resource commitments.

The amount of published international research activity directly or indirectly stimulated by the 1979 Needleman et al. study is huge. This writer found that for 1991 there were well over 1,200 entries in *Chemical Abstracts* dealing with lead toxicity, exposure, and laboratory measurement. The 1991 *Index Medicus* contains over 400 entries for lead toxicology and exposure mainly in humans, while mainly experimental animal lead toxicology entries in the 1991 *Biological Abstracts* number about 600. Over a dozen cross-sectional and three major longitudinal epidemiological studies from around the world have replicated or confirmed Needleman's original neurobehavioral toxicity results. Over a dozen studies also show that lead increases blood pressure in older adults in general and in occupational populations. In addition, many dozens of animal model studies of low-level lead toxicity have been reported in the international literature, including over a dozen neurobehavioral studies in nonhuman primates chronically exposed to low or moderate levels of lead.

Many recent investigators of lead's effects in children have found toxic effects at much lower body lead burdens, e.g., Pb-B, than were probably present in Needleman's subjects. Needleman et al. used shed teeth as a cumulative, more interpretable index of earlier lead exposures in their subjects; translating these measures to Pb-B is difficult. At present, there is a scientific consensus in various international scientific and public health documents that various neurobehavioral and nonneurobehavioral effects are induced in children at a Pb-B of 10 μg/dl or even less [8,12–16].

IMPACT ON ENVIRONMENTAL HEALTH RISK ASSESSMENT ISSUES

In introducing a broad perception of what constitutes lead poisoning in children, Needleman's study helped to establish lead as a prototype for human health risk assessments for toxic environmental pollutants. These include such generic risk assessment elements as:

- What is an adverse health effect?
- Can effects be ranked for biological or societal significance?
- Use of distributions of an adverse effect in a population versus averages, i.e., focusing on subjects at greatest risk via dose or response.
- Subclinical toxicity that is present across an entire population versus overt toxicity present in one or more individuals and the closely related issue of
- Cumulative adverse impact versus individual effects in defining total community health risk.

As I have argued at length elsewhere [17], the traditional criteria for what is an adverse health effect of lead were "clinical" in nature because it was only the high-exposure, clinical end of lead's toxicological spectrum that could be evaluated by the relatively crude diagnostic measures available in earlier times. Because other effects could not be detected by such crude measures, they were assumed not to exist. Methodology determined toxicology. Overt severe effects, crudely measured, were then enshrined in the canons of clinical toxicology as the official adverse effects of lead. However, there is little scientific logic to the notion that an adverse subtle effect measured by sophisticated measures is *inherently* less important than those only measurable by crude means. Does crude *really* equal important?

The Needleman study provoked widespread public health concerns (outside of the usual high-risk focus) for a number of reasons. First, it revealed the potent capacity of lead to impair the brain in the form of reduced cognitive function across the whole child population IQ distribution, particularly to impair IQ in high-IQ children. Second, its findings showed that such effects were at body lead burdens low enough that any parent was justified in suspecting lead exposures. Third, American public sensibility, in theory at least, places a higher premium on protecting child health over the health of other segments of the population. In this regard, public perceptions and scientific criteria for lead's dose-response relationships generally agree. Finally, toxicants such as lead that impair mental acuity engender more alarm in parents and society at large than do toxicants that affect other organs and systems. Why? Whether socially equitable or not, developed cultures clearly appear to equate being human with one's cognitive ability. The brighter the mind, the more "human" the person and vice versa.

The Needleman et al. study found that there was a group mean IQ decrement of four points or so in their subjects. This level of decrement has been called a negligible effect, but that view ignores the fact that there is a distribution of values about any mean value, and, in the case of lead's effects on IQ, Needleman subsequently demonstrated [18] that the impact of a modest average IQ decrement in his subjects translated to major shifts in the tails of the overall IQ distribution—more slow children at the lower end, fewer bright children at the top.

Most environmental toxicants affect a limited segment of people, and the impact must be severe to be recognized, given most data bases. Orthodox risk assessment is still oriented to this scenario. With lead, huge numbers, including millions of children, are affected by relatively subtle adverse effects on IQ, attention, etc. This requires a different risk quantitation approach, wherein one looks at cumulative or society-wide deficits in function of millions or tens of millions. One tack is social cost. Dr. Joel Schwartz, EPA Senior Scientist, MacArthur Fellow, and the world's authority on monetized cost-benefit analyses of regulating different lead sources, has demonstrated benefits over costs of billions of dollars. This approach takes on increasing urgency in a globally competitive world where the entire society must operate optimally.

CHALLENGES TO THE ECONOMIC CENTRALITY OF LEAD

For much of its industrial and commercial history, the American and European lead industry established and maintained a virtual monopoly on research or other investigations of lead's public health and environmental impacts and dissemination of such data [17,19–21]. Put bluntly, the originators of the lead problem also determined who would do what about the lead problem. This was the case for

tetraethyl lead (TEL), a gasoline additive introduced in the mid-1920s.

For more than 40 years, a single biomedical investigator and corporate consultant at the University of Cincinnati not only did most of the research on the health impacts of TEL and combustion of leaded gasoline but also was considered its "official" voice in governmental and institutional scientific circles [19–21]. This monopoly and the influence of the lead industry began to unravel with the growth in independent, non-industry-supported, scientific research in Western countries in the 1960s. It particularly began with the alarming findings of Patterson [22], who showed through elegant techniques that leaded gasoline was producing enormous global lead contamination. The loss of control over information continued with several major developments in the 1970s. First, the U.S. EPA was established, and it began, albeit slowly and reluctantly, to regulate lead in various media. For example, air lead was classified as an ambient pollutant to be regulated nationally. Equally important, the federal government began funding independent research into lead as a toxicological and environmental issue. The 1979 Needleman study was one of the results.

Responses of the lead-producing and lead-using industries and their allies to the growing scientific case against lead constitute a useful case study in how established economic interests react to scientific evidence threatening their activities. Originally, as Needleman notes elsewhere in this issue of the *Quarterly* [1], the bearers of adverse information were seemingly intimidated on an ad hoc, individual basis. When adverse information on lead exposure and human intoxication could not be contained "one-on-one" during the 1970s and 1980s, the industry abruptly took the tack of seeming cooperation. It cultivated a simulacrum of concerned, responsible "objectivity," expanded and established its own research programs and conferences, and heavily intruded into the regulatory evaluation process itself.

Science evolves, but it evolves imperfectly; in its early jerky thrusts at the truth of a matter, there is considerable uncertainty about research results, their meaning, and their consequences. The 1970s and early 1980s typified this period for lead as a scientific research topic, and industry exploited this uncertainty exhaustively and effectively. The multidefense industry position now seemed to say: *Our* experts don't agree that lead exposure has occurred, but if it has *our* experts don't agree that the exposure produces significant public health problems, but if it does *our* experts say it's not extensive enough in the population to worry about. Current industry strategy, having apparently given up on a science that continued to indict lead as a major health issue, apparently relies on economics and cost-effectiveness: Lead is too important an economic commodity to regulate; what's more, the costs of existing lead abatement are too high for the benefits.

Given industry's complex strategy, the Needleman study posed special difficulties. It involved asymptomatic lead poisoning in children with clearly elevated body lead burdens accumulated over the years, two issues especially difficult for the industry. It meant that the scope of lead's harm to cognitive function now extended to countless children in various sectors of society. Lead's cumulative potential for harm redefined what is or is not "harmless" exposure. Numerous research findings over the last 13 years only further compounded the difficulties for the lead industry. Not surprisingly, the industry launched persistent assaults on the Needleman study. In the early 1980s, these included misrepresenting, via wide publicity, technical evaluation of the Needleman study by the EPA's advisory consultants. More recently, the industry has supported efforts of others attacking the Needleman results and Needleman personally. In this regard, suspicion of misconduct charges were filed against him [23]. After an extended investigation of the charges by the University of Pittsburgh, Needleman was cleared of misconduct charges [24,25]. ❧

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